PART I

HYPOLIPIDEMIC ACTIVITY OF *KADUKKAI CHOORANAM* (*Terminalia chebula*)

&

PART II

ANTI-ULCER ACTIVITY OF "MILAGATHY CHOORNAM"

The dissertation Submitted by

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Hypolipdemic Activity of *Kadukkai Chooranam (Terminalia chebula)* and Anti Ulcer Activity of *Milagathi chooranm*"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.M.Pitchiah Kumar, MD (s)** and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

Date:

Signature of the Candidate

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ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **““Hypolipdemic Activity of *Kadukkai Chooranam (Terminalia chebula)* and Anti Ulcer Activity of *Milagathi chooranm*”** is a bonafide work carried out by F.Priya under the guidance of **Dr.M.Pitchiah Kumar, MD (s)** Post Graduate Department of Gunapadam, Govt.Siddha Medical College, Arumbakkam, Chennai-106

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BONAFIDE CERTIFICATE

Certified that this thesis entitled **"Hypolipidemic activity of *Kadukkai Choornam*(Terminalia chebula) and Anti-ulcer activity of Milagathi Choornam"** is the bonafide work of **Dr. F. Priya (Reg No.32101609)** who carried out the dissertation work under my supervision. Certified further, that to the best of my knowledge the work reported here-in-does not form part of any other thesis or dissertation on the basis of which a degree or award was conferred on an earlier occasion on this or any other candidate.

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Introduction

HYPOLIPIDEMIC ACTIVITY OF KUDIKKAI SHOORNAM

The *Siddha* system of medicine is contributing much more the health care of human society. This system is developed by *siddhars* who are the great scientists of ancient days. Generally the *siddhars* are considered to be super-human beings who have defined age and other laws of nature to which all human beings are subject to. *Siddhars* have developed longevity discipline called *kayakalpa*. *Kayakalpa* is the crown of *siddha* system as it is not mentioned in any other system of medicine.*Kaya* means body. *Kalpa* means rejuvenation. It is a legendary system of whole body rejuvenation.

Kayakalpa has following objectives

1.Maintaining youthfulness and physical vigor

2. Withstanding the ageing process and promotes longevity

3 .Live a full span of quality life

The approach is not only towards physical immortality (which on some deeper level of harmony may be possible), but the immortality of the mind, the daily renewal of brain cells. In such state, the mind and heart are as clear in old age as in childhood.

The medicines that are used to make this, the process of doing, diet to be followed; timings to eat all these have been clearly explained by the *siddhars* in their medical scripts.

Ever since men started curing illness, he began to discover the causes for illness. Then prevention of illness was also added in evolution of culture. In his efforts to cure and prevent illness he further thought over the postponement of death. *Siddhars* were successful in their research and lived as long as they wished

The *siddhars* were a class of popular writers in Tamil in all its branches of knowledge and many of their work were written in what is called high Tamil. The *kavi* or poetry in which the medical and other scientific tracts have been composed is much admired by those who have made it their special studies.

Kayakalpa has been told by Thirumoolar as

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Herbal medicine can be used to treat, to enhance treatment or to alleviate side effects of other system of medicines. India is one of the largest producer of medicinal herbs and is rightly called the "Herbal Garden Of The World." Rising interest in herbal medicine reflects the public's attempt to create a more gentle ecologically sensitive medicine that has been created with technology based medicine.

Cholesterol, a steroid makes up an important part of the membranes of each cell in the body. Our body also uses cholesterol to make bile acid, vitamin D and some hormones. Even though it is beneficial, high levels of cholesterol in the blood leads to hyperlipidemia a major risk factor for ischemic heart disease and cerebrovascular diseases. "Higher the cholesterol greater the risk of Coronary Artery Disease"- KD.Tripathi; Medical pharmacology-sixth edition-2010. Faulty diet particularly with an increase inclination towards fast food, which are rich in saturated fats, lack of exercise, increase time spent on watching TV, increase car ownership, increase automation, decrease manual labour in the developing countries are some of the reasons for hyperlipidemia.

Cardio vascular disease prevalence in India has risen four-fold in the past four decades. Expected to be the leading cause of death and disability by 2020, Cardio vascular disease already causes 29% of all deaths in the country. "Indians are succumbing to heart disease and stroke in the most productive years of their lives; about a decade earlier than their western counterparts" said Dr KS Reddy, President of the Public Health Foundation of India.

With the etiological prominence of hyperlipidemia in Coronary heart disease and cerebrovascular disease various drugs have been utilized to lower the blood lipids such as clofibrate, niacin, statin and gemfibrozil. All though these drugs

were successful in reducing the serum cholesterol levels, they produce unpleasant and distressing side effects such as depression, myalgia etc. So a safe and effective herbal medicine will provide better result for this condition.

Kadukkai (*Terminalia chebula*) is one of the herbal *kayakalpa* according to *karuvurar vadha kaviyam.* It is a tropical tree which is found growing at attitudes upto 650 meters possess a great trunk with thick leaves and has yellowish flowers and blackish yellow or blackish-brownish fruits. The fruit is used in medicine, the seed is taken out and the whole pulp is used.

Kadukkai is a rejuvenative, laxative (unripe), astringent (ripe), anthelmintic, nervine tonic, expectorant, tonic, appetite stimulant, easily assimilated, anti-septic, alterative, diuretic and carminative. It promotes digestive power, heals wound and ulcers, cures local swellings, skin diseases, diabetes, chronic and recurrent fever, anaemia, diarrhoea, dysentery, cough and dyspnoea. It dispels disease caused by vitiation of vatha, pitha and kapha and is useful in spleen enlargement, ascites, piles, hoarseness of voice, vomiting and hypertension.

The major constituents are tannins, chebulagic acid, chebulinic acid, ellagic acid, gallic acid, anthraquinones,vit c, chebulic acid, oleic acid, palmitic and stearic acid

Kadukkai has five of 6 tastes, only the saline taste is missing. An example of siddha recipe containing *kadukkai* is *Agastiya Rasayana*, a famous tonic. This formula was created by the sage *Agathiyar*, the original profounder of *siddha* system of medicine. According to *Agathiyar, kadukkai* is compared to mother but he describes that eventhough *kadukkai* is compared to mother, it seems to be more than mother in the sense, mother feeds the baby and provide nourishment but *kadukkai* drive away the diseases and provides nourishment too.

Kadukkai promotes long life, rejuvenates and stimulates enzymatic action. Phytosterols and natural antioxidants have also been shown to be effective in reducing lipid profiles and also lessen peroxidative modification of lipoproteins and atherosclerosis. Since *kadukkai* contains high amounts of phytosterols, saponins, chebulinic acid and corilagen, it will be a promising phytomedicine for hypolipidemic activity. In that basis, it will be an excellent drug for hypolipidemic activity.

Aim & Objectives

CHAPTER I

1. Aim :

To validate the safety and efficacy of *Kadukkai Choornam* in the management of Hyperlipidemia.

2. Objectives:

In this dissertation work, the ***"KADUKKAI CHOORANAM'*** is analyzed in the following aspects:

- Standardization of *Kadukkai choornam* including pharmacognostic characterization of raw drug and purity analyses
- Safety profile for the test drug in rat
- Pharmacological study to evaluate the hypolipidemic activity in rat
- Open clinical study to assess the safety and efficacy of the drug on hyperlipidemic patients.

Review of Literature

CHAPTER II REVIEW OF LITERATURE

1.Drug review

Botanical aspect of the plant

Botanical name: *Terminalia chebula* (Gaertn) Retz

Classification

Kingdom	:	*Plantae*
Subkingdom	:	*Tracheobionta*
Superdivision	:	*Spermatophyta*
Division	:	*Magnoliophyta*
Class	:	*Magnoliopsida*
Subclass	:	*Rosidae*
Order	:	*Mirtales*
Family	:	*Combretaceae*
Genus	:	*Terminalia*
Species	:	*chebula*

Vernacular names

English	:	*Chebulic Myrobalan*
Tamil	:	*Kadukkai*
Sanskrit	:	*Haritaki, priya, sudha*
Hindi	:	*Pile Hara*
Pers	:	*Haleelai Siah*
Kan	:	*Anile-Kayl*
Tel	:	*Chitti karakkaya*
Mal	:	*Katukkaipinja*

Hippocrates said that if one bites a piece of Chebulic Myrobalan after meals and swallow its juice, one will remain free from all diseases. *Kadukkai* chewed in the morning everyday in empty stomach heals a number of ailments like piles, colitis, skin eruptions, constipation, voice disorders, asthma, defective vision, wounds, acidity, gall stones etc. The most important point to remember is that it increases

longevity. It is said to be a good liver tonic. (Ref: Fruit and vegetable juice therapy - N.N.Saha2002)

D**escription**

It is a large deciduous tree 15-24m in height and 1.5 to 2.4m in girth with a cylindrical bole of 4-9m, a rounded crown and spreading branches, found throughout the greater parts in India. Bark dark- brown often longitudinally cracked, exfoliating in woody scales; leaves are mostly sub opposite, ovate or elliptic with a pair of large glands at the tip of the petiole: flowers are dull, white or yellow, small scented in terminal, paniculate spikes, drupes ellipsoidal, obovoid or ovoid yellow to orange brown, sometimes tinged with red or black and hard when ripe, 3-5cm long, become 5 ribbed on drying, seeds hard, pale yellow. Based on fruit size and shape it has as many as seven types. Flowering / Fruiting- April to June/January to March. (Wealth of India volume 3)

Parts used- Fruits

The mature (ripe) haritaki fruits are harvested during the autumn season, when they have the strongest medicinal and laxative effect. Drying the fruit properly in the sun to make a powder reduces the laxative effect slightly, and cooking or steaming reduces it even further, due to oxidation of the laxative chemicals. Traditional doctors disapprove of cooking the fruit when it should be sun-dried (a tedious process). The cooking process is thought to weaken the herb's medicinal effectiveness. (Medicinal and Aromatic Plants of HP - Narain Singh Chauhan 1999).

Materia Medica

Chebulic myrobalan fruit embodies all tastes except salt. It is good for health and long life. It is also tridosagna, meaning it can be used with any type of health imbalance. Furthermore, it is a mild laxative that aids digestion. *Kadukkai* is used to nourish the heart, liver, and kidney, and to treat diseases of the eye, for which it is used both internally and externally.

Types

According to siddha it is classified into seven types. They are

Vijaya: looks just a squash and can be used in any case.

Rohini: is round in shape and more effective for healing.

Putana: is small in size with big hard seeds, and is useful for external plastering.

Amrita: is fleshier, and good for body purification.

Abhaya: has five lobes, and is more effective for ophthalmic use (external).

Jivanti: is yellow in colour and good for all cases.

Chaetaki: has three lobes, is good to use in the form of powder, and is more laxative than the others. Chetaki comes in two varieties - white and black.

General character

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Kadukkai cures the diseases of the Cheek, neck, tongue and penis. It is said to be a potent drug for obesity and cures jaundice, herbal and animal poison.

A decoction of chebulic myrobalan is a good astringent. Wash useful in bleeding piles and some vaginal discharges.

Finely powdered *kadukkai* is used as a dentifrice useful in carries teeth, bleeding and ulceration of gums.

Coarsely powdered and smoked in a pine it affords relief in a fit of asthma.

Equal parts of *kadukkai* and *kasukatti* rubbed into a paste and applied for tongue ulcer.

Unriped fruit is rubbed with milk given internally for cough.

In folk medicine, *kadukkai* is used in constipation, tympanitis, vomiting, colic, sprue syndrome, jaundice, splenic disorders, for treating cough, asthma, hiccup, throat affections, and impaired voice.

One fruit of *kadukkai (Terminalia chebula)*, two fruits of *thantrikkai (Terminalia bellerica)*, and four fruits of *nellikkai (Emblica officinalis)* taken together, were called *Triphala.* It is prescribed as a laxative, digestive, promoter of eyesight, intellect and longevity. It is credited with the properties which enhance body resistance against diseases and induce immunity; and is included as an adjunct in a number of compound preparations.

The main purgative ingredient of *Triphala* is *T.Chebula,* possibly by rendering the irregular peristaltic movements uniformly progressive. The purgative principle in the pericarp of the fruit of *T.chebula* has been found to be a glycoside which may be similar to sennoside A (Wealth of India)

The presence of a non-nitrogenous neutral principle in the fruit, named chebulin, possessing anti spasmodic activity similar to that of papaverine has been reported (Gaind et. al, Indian J Pharm,1964,26,10)

Triphala is used in folk medicine, as a dentrifrice for bleeding gums. Mixed with oil, it is applied to cuts, wounds, burns and scalds. Water, in which *Triphala* has been steeped overnight, is used as a cooling wash for eyes. Also for affording relief in conjunctivitis.

Triphala also used as adjunct to other medicines in numerous disease.

Haritaki fruit contains anthraquinone - like (laxative) chemicals as well as tannins and astringents (reported in Kapoor, 1990). To bring out these opposing actions within a given product, *siddha* doctors administer it with warm water to strengthen the laxative action, and with ice cold water to promote the astringent action. For example, the juice mixed with cold water can be used as a mouthwash to treat spongy gums.

The post - digestive or delayed reaction of *haritaki* fruit *(vipaka)* is very strongly nourishing, so this is an excellent choice as a laxative in weak or elderly patients. [One earth herbal source book - Herbalist Alan Tilotson]

Haritaki fruit is part of *triphala,* the three-fruit formula. It is generally administered in *triphala* form rather than by itself to draw upon the tonic effects. Each of the *triphala* fruits is tonic, and together they act to balance the three primary balancing forces, *Vata, Pitta* and *Kapha.*

Dried or cooked *haritaki* fruit tighten up the stool for chronic diarrhoea and dysentery. By stating that it can be used for both hot and cold patterns of disease, they are acknowledging the balanced action of this herb.

ACTIVE PRINCIPLES AND PHARMACOLOGY

Fruit contain chebulinic acid, tannic acid and chebulin. Oil from kernels yielded palmitic, searic, oleic, linoleic, arachidic and behenic acids.

Antioxidant constituents of the plant, phloroglucinol and pyrogallol, have been isolated along with ferulic, vanillic, p-coumaric and caffeic acids. Acid esters present in phenolic fraction of extract were found more effective.

A new ellagitannin-terchebulin-has been isolated from fruits along with punicalagin and terflavin A and its structure has been elucidated. Terflavins B, C and D, punicalagin and punicalin have been isolated from leaves.

Gallic, triacontanoic and palmitic acids, beta-sitosterol, doucosterol, ethyl ester of gallic acid from fruits have been isolated. A new triterpene - chebupentol-has been isolated from fruits; arjungenin, terminoic acid arjunolic acid have been isolated.

The oil in the kernel increased the motility of the gastrointestinal tract of the mouse. The action was comparable with castor oil. The oil itself is non irritant, but releases an irritant principle when incubated with lipase. (Indian herbal remedies C.P.Khare 2004)

Research Highlights

- kadukkai fruit extract was tested as a mouth rinse to study its effect on bacterial growth. It significantly inhibited salivary bacterial count and total streptococcal mutans count (Jagtap and Karkera, 1999).
- Kadukkai fruit was one of six traditional herbs administered to animal to test their adaptogenic potential. All six traditional rasayana plants were able to aid

the animals against a variety of different stressors working in different ways (Rege, 1999).

- Alcohol extract of chebulic myrobalan was tested in vitro against several pathogenic and opportunistic microorganisms. It had a broad spectrum as well as potent action. Subsequent animal testing showed no cellular toxicity (Ahmad *et al.,* 1998).
- Tests of alcohol extracts revealed gallic acid and its ethyl ester, two potent antimicrobial substances that acted against even resistant strains of Staphylococcus aureus (Sato *et al.,* 1997)

  Chebulic myrobalan significantly reduced the viral loads in a chronic lung infection (CMV) which is common in AIDS patients (Yukawa *et al.,* 1996).
- Haritaki fruit was one of four herbs screened out for potency to test for use with the anti-viral drug acyclovir against herpes (HSV-1) in a study at the Toyama Medical and Pharmaceutical University in Japan. When acyclovir was combined with any one of the herbal extracts and ingested in oral doses similar to human use, the results were significantly stronger than the use of the drug or the herbs alone, especially reducing viral loads in the brains of the animals (Kurokawa *et al.,* 1995).

Current scenario of research in *Kadukkai*

Antioxidant Effects of Aqueous Extract of *Terminalia chebula in Vivo* and *in Vitro*

The objective of this study was to evaluate the protective effects of an aqueous extract of fruit of T. chebula on the tert-butyl hydroperoxide (t-BHP)-induced oxidative injury observed in cultured rat primary hepatocytes and rat liver. Both treatment and pretreatment of the hepatocytes with the T. chebula extract (TCE) significantly reversed the t-BHP-induced cell cytotoxicity and lactate dehydrogenase leakage. (Hyun-Sun LEE, et, al)

Inhibition of cancer cell growth by crude extract and the phenolics of *Terminaliachebula* retz. Fruit Journal of Ethnopharmacology

A 70%methanol extract of *Terminalia chebula* fruit, was studied for its effects on growth in several malignant cell lines including a human (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human

prostate cancer cell line (PC-3) and a non-tumorigenic, immortalized human prostate cell line (PNT1A) using assays for proliferation ([H]-thymidine incorporation and coulter counting), cell viability (ATP determination) and cell death (flow cytometry and Hoechst DNA staining). In all cell lines studied, the extract decreased cell viability, inhibited cell proliferation, and induced cell death in a dose dependent manner. (1 August 2002, Pages**,** Ammar Saleem et.al)

Antibacterial activity of black myrobalan (*Terminalia chebula.* Retz) against *Helicobacter pylori,* International Journal of Antimicrobial Agents, Volume 18, Issue 1, July 2001, F Malekzadeh **,** et, al

- The effect of ether, alcoholic and water extracts of black myrobalan (*Teminalia chebula.* Retz) on *Helicobactor pylori* were examined using an agar diffusion method on Columbia Agar. Water extracts of black myrobalan showed**,** significant onantibacterial activity and had a minimum inhibitory concentration (MIC)

Influence of *Terminalia chebula* on dermal wound healing in rat

Lonchin Suguna, et, al *T. chebula* treated wounds healed much faster as indicated by improved rates of contraction and a decreased period of epithelialization. Biochemical studies reveled a significant increase in total protein, DNA and collagen contents in the granulation tissues of treated wounds.

Journal of health science

Anti-Diabetic Activity of Fruits of *Terminalia chebula* on Streptozotocin Induced Diabetic Rats

Oral administration of ethanolic extract of the fruits (200 mg/kg body weight/rat/day) for 30 days significantly reduced the levels of blood glucose and glycosylated hemoglobin in diabetic rats. (Gandhipuram *et al.*,)

Antioxidant and Free Radical Scavenging Activities of *Terminalia chebula*

Free radicals react with biological molecules and destroy the structure of cells, which eventually causes free-radical induced disease such as cancer, renal failure, aging, *etc*. The results showed that all tested extracts and pure compounds of *T. chebula* exhibited antioxidant activity at different magnitudes of potency.(Hua-Yew Cheng, et, al)

Medicinal preparations of *Kadukkai*

1.Kadukkai nei

Kadukkai - *100gm*

Keezhkai nelli - *700gm*

Kadukkai, keezha nelli are crushed and decoction is prepared. *Katakarogini, kadukkai, thippili* each 17.5gm, are ground and add with above decoction.Then ghee 1 padi is added, boiled and filtered.

Dose : 10.2 gm twice daily.

Uses : Obesity, indigestion, constipation, pitham.

Ref : *Pathinen Siddhar Arulia Aavialikum Amutha Murai Churukkam, V.Kanthaswamy Muthliar*

2.Kadukkai Karpam

Prepararation : Kadukkai is powdered finely and bottled.

Dose : 1gm twice daily

Uses: Jaundice precaution

3.Kadukkai Legium

Preparation*:* *Kadukkai* 350 gm crushed.Water two marakkal to be added, boiled, reduced to 1/8 part and the decoction is strained in a vessel. 350 gm sugar is dissolved and boiled into a syrup. In that sivadhai, ginger, pepper, omam vaividangam ,thippili each 35gm ground well and added. Ghee 1padi added and mixed in order to make the consistency of the medicine as that of legium.

Dose : 5gm twice daily

Uses : Constipation, flatulence, piles,

Other medicines which containing Kadukkai

Komoothira Silasathu parpam

Preparation : *Kadukkai, thantrikkai nellimulli* each 35gm taken. Water 4 saer added,

boiled and reduced into 1/4 part. 1/4 saer silsathu is rubbed in a kalvam,

villais are made dried and subjected to putam with 1000 varaties. It become a fine parpam.

Uses : Tuberculosis, chronic fever.

Ref : Sarabendira vaidhya rathnavali

Karpoora Siasathu Choornam

Preparation :

Paereechu - 48gm

Nelliparuppu - 48gms

Thippili - 48gms

Karrpoora silasathu - 48gms

Ealam - 48gms

Athimathuram - 48gms

Kadukkai - 48gms

Vengaram - 48gms

Sandanam - 48gms

Vellari vidai - 48gms

Thania vidai - 48gms

All the above drugs are powdered and sieved

Dose : 1/2gm twice daily

Uses : Mega diseases, ratha pramium, seezh pramium

Ref : *Agathiyar attavanai vagadam*

Amalathi Girutham

Amla juice - *1padi,*

Sugarcane juice - *1padi*

Ghee - 350gms

Kadukkai powder - 87gms

Preparation

Kadukkai is powdered and rubbed nicely with the help of any one of the above juice. All are mixed well in a mud pot boiled until to get the correct consistency

Dose : Two tea spoon, two times a day.

Uses : Ulcer, Vomiting, Burning chest.

Ref : *Sihicha Rathna Deepam*

2.Disease review-Obesity

Obesity is an abnormal accumulation of body fat, usually 20percent or more over an individual`s body weight. (1) Discrepancy between energy consumption and the energy expenditure ended up with accumulation of fat. A continuous intake of 50 to 200 calories extra per day would lead to weight gain of 2-20kg over a period of 4-10 yrs. Given the cumulative effects of subtle energy, excess body fat content shows `tracking` with age such as obese children usually become obese adults.

Some reasons for increasing prevalence of obesity are increased energy intake, increased portion sizes, increased snacking and loss of regular meals, increased energy dense food, increased affluence.

Decreased energy expenditure

Increased car owner ship, decreased walking to school, increased automation, decreased manual labour, decreased sports in schools, increased time spent on computer games and watching TV.

A few rare single gene disorders have been identified which lead to severe childhood obesity. These include mutations of the melanocortin-4receptor (MC4R)

that accounts for approximately 5% of severe early-onset of obesity Mutations in the leptin gene.

Reversible Causes of Obesity

Endocrine factors such as hypothyroidism, cushings syndrome, insulinoma, hypothalamic tumours or injury.

Measurement of obesity

Severity of obesity can be quantified using the BMI. A waist circumference of >102cm in men or >88cm in women indicates that the risk of metabolic and cardiovascular complications of obesity is high.

Quantifying obesity with body mass index

BMI(kg/m)	Classification	Risk of obesity comorbidity
18.9-24.9	Normal range	Negligible
25.0-29.9	Over weight	Mildly increased
>30.0	Obese	
30.0-34.9	ClassI	Moderate
35.0-39.9	ClassII	Severe
>40.0	ClassIII	Very severe

[1]

Hyperlipidemia-is major risk factor for atherosclerosis; even in the absence of other factors, hypercholesterolemia is sufficient to stimulate lesion development. The major component serum cholesterol associated with increased risk is low density lipoprotein (LDL) cholesterol ("bad cholesterol"). LDL cholesterol is the form of cholesterol that is delivered to peripheral tissue. In contrast, high density lipoprotein (HDL, "good cholesterol") mobilizes cholesterol from tissues and transport it to the liver for excretion in the bile. Consequently, higher levels of HDL correlate with reduced risk. High dietary intake of cholesterol and saturated fats (present in egg yolks animal fats and butter, for example) raises plasma cholesterol levels. Conversely, diets low in cholesterol and with higher ratios of poly unsaturated fats lower plasma cholesterol levels. Omega 3fatty acids (abundant in fish oils) are beneficial, whereas trans-unsaturated fats produced by artificial hydrogenation of

polyunsaturated oils (used in baked goods and margarine) adversely affect cholesterol profiles. Exercise and moderate consumption of ethanol raise HDL levels, whereas obesity and smoking lower it. (Robbins and cotran pathology of disease)

Dietary lipids are absorbed in the intestine with the help of bile acids. Chylomicrons are formed and passed into lacteals - reach blood stream via thoracic duct. During their passage through capillaries, the endothelium bound lipoprotein lipase hydrolysis the TGs into fatty acids which pass into muscle cells to be utilized as energy source and in fat cells to be reconverted into TGs and stored. The remaining part – chylomicron remnant containing mainly cholesterol ester and little TG engulfed by liver cells, which have receptors for the surface apoproteins of chylimicron remnant and digested. Free cholesterol that is liberated is either stored in the liver cells after reesterification or incorporated into a different lipoprotein and released in blood or excreted in bile as cholesterol /bile acids

Liver secretes very low density lipoprotein (VLDL) containing mainly TG and some cholesterol ester and some cholesterol into blood. VLDL is acted upon by endothelial lipoprotein lipase in the same way as on chylomicrons and the fatty acids pass into the adipose tissue and muscle; the remnant called intermediate density lipoprotein (IDL) now contains more cholesterol esters than triglycerides. About half of the IDL is taken back by the liver cells by the attachment to another receptors (LDL receptor), while the rest loses the remaining triglycerides gradually and becomes low density lipoprotein (LDL) containing only clolesterol ester. The LDL circulates in plasma for a long time; its uptake into liver and other tissues is dependent on the need for cholesterol. The rate of LDL uptake is regulated by the rate of LDL receptor synthesis in a particular tissue.

The cholesterol ester of LDL is de-esterified and used mainly for cell membrane formation. The cholesterol released into blood from degradation of membranes is rapidly incorporated in high density lipoprotein (HDL), esterified with the help of an enzyme lecithin. The excess lipoproteins in plasma are phagocytosed by macrophages for disposal. when too much of lipoproteins have to be degraded in this manner. Cholesterol is deposited in atheroma (in arterial walls) and xanthomas (in skin and tendons)- (Tripathy)

Material & Methods

CHAPTER III MATERIAL AND METHODS

1. STANDARDIZATION OF KADUKKAI CHOORNAM

1.1 Collection and authentication of raw drug:

Fresh fruits of Kadukkai were collected during the month of June (2012) from Kollimalai, Salem Dist, Tamilnadu, India and dried well. The dried raw drug was authenticated by the botanist, Siddha Central Research Institute, Chennai and also from the experts in the Department of PG Gunapadam, Govt. siddha medical college, Chennai-106 by correlating the macroscopic characters with the specimen kept in the department.

1.2 Macroscopic and microscopic studies of test drug

Outer Coat

For examining the outer coat, 3 fruits were boiled in caustic alkali solution in a test tube for 1-2 minutes. After boiling, the pieces were placed on slide, the layers of the coat were removed and examined them after mounting in glycerol solution.

Sectioning

The pericarp of the fruits were boiled for 15 minutes and cut into small peices for examining purpose. Then, it was fixed in FAA (Formalin-5ml+ Acetic acid-5ml + 70% Ethyl alcohol-90ml). After 24 hrs of fixing, the specimens were dehydrated with graded series of tertiary – Butyl alcohol as per the schedule given by Sass, 1940. Infiltration of the specimens was carried by gradual addition of paraffin wax (melting point 58-60 C) until TBA solution attained super saturation. The specimens were cast into paraffin blocks. The paraffin embedded specimens were sectioned with the help of Rotary **Microtome.** The thickness of the sections was 10-

12 μm. Dewaxing of the sections was done by customary procedure (Johansen, 1940). The sections were stained with **Toluidine blue** as per the method published by O'Brien et al (1964). Since, **Toluidine blue** is a polychromatic stain, the staining results were remarkably good; and some **cytochemical** reactions were also obtained. The dye rendered pink colour to the **cellulose** walls, blue to the **lignified** cells, dark green to suberin, violet to the mucilage, blue to the **protein** bodies etc. wherever necessary sections were also stained with **safranin** and **Fast-green** and IKI(for Starch).

Photomicrographs

Microscopic descriptions of tissues are supplemented with micrographs wherever necessary. Photographs of different magnifications were taken with Nikon lab photo 2 microscopic Unit. For normal observations bright field was used. For the study of crystals, starch grains and lignified cells, polarized light was employed. Since these structures have bi refringent property, under polarized light they appear bright against dark background. Magnifications of the figures are indicated by the scale-bars. Descriptive terms of the anatomical features are as given in the standard Anatomy books (Esau, 1964).

1.3 Preparation of *Kadukkai choornam*

Kadukkai choornam was prepared by the method described in page no. 207, Siddha Materia Medica – Medicinal plants division (Murugesha 2008). The pericarp of *Kadukkai* fruits were collected by removing the seeds. The well dried pericarps were made into very fine powder by grinding in pulveriser and filtered through the mesh of the sieve size no. 125. The fine powder was subjected for purification by the *pittaviyal* method. The powder was moistened with cow's milk. The pot was half filled with milk and water. The mouth of the pot was covered with

white cotton cloth. The powder (moistened by milk) was placed above the cloth. The mouth of the pot closed with another mud pot. The gap between the two mud pots was tied with a wet cloth to avoid evaporation. Then, this arrangement was put on fire and boiled until water level gets reduced in the lower pot. Then, the powder was taken out, and dried, and powdered finely, and preserved in an air tight container. The expiry period of *Kadukkai choornam* has been for 3 months. It should be used within that period.

1.4 Physico chemical analyses

1.4(a) Physico chemical parameters

Determination of Total Ash

3 g of the powder was incinerated in a silica dish at a temperature not exceeding 450º until free from carbon, cool and weigh. The percentage of ash was calculated with reference to the air-dried drug.

Determination of Acid Insoluble Ash

The obtained ash was boiled for 5 minutes with 25 ml of dilute hydrochloric acid and insoluble matter was collected in ashless filter paper. Then, it was washed with hot water and ignited to constant weight. The percentage of acid-insoluble ash was calculated with reference to the air dried drug.

Determination of Alcohol Soluble Extractive

5 g of powder was mixed with 100 ml of Ethanol of the specified strength in a closed flask and kept alone for twenty-four hours. Filtered rapidly with taking precautions against loss of solvent. 25 ml of the filtrate was evaporated to dryness in a tared flat bottomed shallow dish, and dried at 105º, to constant weight and weighed. The percentage of alcohol-soluble extractive was calculated with reference to the air-dried drug.

Determination of Water Soluble Extractive

5 g of powder was mixed with 100 ml of chloroform water of the specified strength in a closed flask and kept alone for twenty-four hours. Filtered rapidly with taking precautions against loss of solvent. 25 ml of the filtrate was evaporated to dryness in a tared flat bottomed shallow dish, and dried at 105º, to constant weight and weighed. The percentage of water-soluble extractive was calculated with reference to the air-dried drug.

Determination of Moisture Content (Loss on Drying)

10 g of drug was taken in the tared evaporating dish and dried at 105º for 5 hours, and weighed. (Continue the drying and weighing at one hour interval until difference between two successive weighing corresponds to not more than 0.25 per cent. Constant weight is reached when two consecutive weighing after drying for 30 minutes and cooling for 30 minutes in a desiccator, show not more than 0.01 g difference).

***Potential of Hydrogen* (pH)**

The pH scale is logarithmic and runs from 0.0 to 14.0 with 7.0 being neutral. Readings less than 7.0 indicate acidic solutions, while higher readings indicate alkaline or base solutions.

1.4(b) THIN LAYER CHROMATOGRAPHY

Solvent system

Toluene : Ethyl acetate: Acetic acid (5 : 5 : 0.5).

TLC plate

Aluminium plate precoated with silica gel $60F_{254}$ of 0.2 mm thickness (Merck).

Developing chamber

Camag's twin trough chamber.

Visualizing reagent

Vanillin-sulphuric acid reagent.

Extract Preparation

4 g of the chooranam was soaked overnight in chloroform. Boiled on a water bath for 10 mins, filtered and concentrated to 10 ml.

Procedure

The extract was applied on the TLC using capillary and developed in the solvent system. The developed TLC plate was air dried and photograph was taken in white light. Then dipped in vanillin-sulphuric acid reagent, heated in an oven at 105°C until the development of coloured spots and photograph taken.

1.4 (c). Qualitative Phytochemical Analysis:

S.No	EXPERIMENT	OBSERVATION	INFERENCE
1.	**Test for Alkaloids:** Alkaloids are identified by precipitate method **Dragendroff's reagent:** An aqueous plant extract of 2 ml is mixed with 2 ml of Dragendroff's reagent.	Absence of reddish brown precipitate	Absence of alkaloids
2.	**Test for Triterpenoids (Noller's Test)** To few mg of extract, add tin and thionyl chloride and heat in water bath.	Absence of purple colour	Absence of Triterpenes
3.	**Test for Tannins:**A plant sample dried powder 0.5 gm is boiled in 20 ml of water and	Forms a brownish-green or bluish- black	Presence of

	filtered. The filterate 2 ml is taken and 3-5 drops of $Fecl_2$ (0.1%) is slowly added to it.	colour.	Tannins
4.	**Test for Flavonoids:** An aqueous filterate of plant sample is mixed with 5 ml of dilute Ammonium solution and few drops of concentrated H_2SO_4 is slowly added through the sides of the test tube.	Absence of Yellow colour formed	Absence of flavonoids
6.	**Test for Glycosides:**An aqueous plant extract of 2 ml is added with 1 ml of concentrated Hcl and boiled in a water bath for about 2 hours. The filtrate is separated and 3 ml of chloroform is added, then 10% of 1ml Ammonium solution is added.	Absence of pink colour formation	Absence of glycosides
7.	**Test for Saponin:** A powdered 2 gm of plant sample is boiled with 20 ml of distilled water, then filtered, the filterate is added with fresh 5 ml of distilled water and shaken vigorously.	A permenant or persistant froth is formed.The froth is turned in to emulsion by adding three drops of olive oil.	Presence of saponin
8.	**Test for Phenolic compounds:** About 2 ml of aqueous plant extract is mixed with 2 ml of $Fecl_3$ solution.	Presence of deep bluish green colour	Presence of phenolic compounds

Methodology for Chemcial Analysis

Preparation of Extract :

Add 5 gm of the sample to 50ml of distilled water. Boil the solution for 20 minutes, cool and then filter. Use the Extract for the following tests.

S.No	Experiment	Observation	Inference
1.	**Test for reducing Sugar :** To 5ml of Benedicts qualitative reagent, add 10 drops of extract, then boil for two minutes	Green / Yellow / Red PPT	Presence of Reducing Sugar
2.	**Test for Starch :** To 5 ml of extract add 2ml of acetic acid and then add few drops of N/50 Iodine Solution.	Blue Colour	Presence of Starch
3.	**Test for Proteins :** To 2 ml of extract, add 2ml of 5% Sodium Hydroxide mix and add 2 drops of Copper Sulphate Solution.	Violet or Purple Colour	Presence of Proteins
4.	**Test for Amino Acid :** Place 2 drops of extract on a filter paper and allow to dry well. Then spray 1% ninhydrin over the same and allow to dry.	Violet Colour	Presence of Amino Acid
5.	**Test for Albumin :** To 2 ml of extract, add 2ml of Esboch's reagent.	Yellow PPT	Presence of Albumin
6.	**Test for Phosphate :** To 2ml of extract, add 2ml of ammonium Molybdate solution and 2ml of concentrated Nitric	Yellow PPT	Presence of Phosphate

	Acid.		
7.	**Test for Sulphate :** To 2 ml of extract add 2ml of 4% ammonium oxalate solution.	White PPT	Presence of Sulphate
8.	**Test for Chloride :** Add 2ml of extract to dilute nitric acid till the effervescence ceases. Then add 2 ml of Silver Nitrate Solution.	Cloudy White PPT	Presence of Chloride
9.	**Test for Iron :** To 2ml of extract, add 2ml of ammonium thio cynate solution and add 2ml of concentrated Nitric Acid.	Red Colour	Presence of Iron
10.	**Test for Calcium :** To 2 ml of extract, add 2 ml of 4% ammonium Oxalate Solution.	White PPT	Presence of Calcium
11.	**Test for Sodium :** Make a paste with 2 pinches of the sample with Hcl and Introduce it into the blue flame.	Yellow Flame	Presence of Sodium
12.	**Test for Potassium :** Add a pinch of the sample to 2 ml of Sodium Nitrate Solution. Then add 2ml of Cobal Nitrate in 20% acetic acid.	Yellow PPT	Presence of Potassium
13.	**Test for Zinc :** To 2ml of extract, add few drops of Sodium Hydroxide.	White PPT	Presence of Zinc

14.	**Test for Magnesium :** To 2ml of extract, add few drops of Sodium Hydroxide Solution	White PPT	Presence of Magnesium
15.	**Test for Alkaloids :** a. To 2ml of extract, add 2ml of Potassium Iodide Solution b. To 2ml of extract add 2ml of Picric Acid. c. To 2 ml of extract add 2ml of Phosphotunqstic Acid.	Red Colour Yellow Colour White PPT	Presence of Alkaloids Presence of Alkaloids Presence of Alkaloids
16.	**Test for Tannic Acid :** To 2ml of extract add 2 ml of Ferric Chloride Solution	Black PPT	Presence of Tannic Acid

1.4 (d) FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR):

INSTRUMENT DETAILS:

Model : Spectrum one: FT-IR Spectrometer

Scan Range : MIR 450-4000 cm-1

Resolution : 1.0 cm-1

Sample required : 50 mg, solid or liquid.

Fourier Transform Infrared Spectroscopy (FTIR) is an analytical technique used to identify mainly organic materials. FTIR analysis results in absorption spectra which provide information about the chemical bonds and molecular structure of a material. The FTIR spectrum is equivalent to the "fingerprint" of the material and can be compared with cataloged FTIR spectra to identify the material.

Infrared spectrum is useful in identifying the functional groups like -OH, -CN, -CO, -CH, -NH2, etc. Also quantitative estimation is possible in certain cases for chemicals, pharmaceuticals, petroleum products, etc. Resins from industries, water and rubber samples can be analyzed.

1.4(e) SCANNING ELECTRON MICROSCOPE (SEM):

The Scanning Electron Microscope (SEM) is a microscope that was electrons rather than light to form an image. There are many advantages to using the SEM instead of a light microscope.

Resolution : 1.2 nm gold particle separation on a carbon substrate

Magnification : From a min of 12 x to greater than 1, 00,000 X

The SEM has a large depth of field, which allows a large amount of the sample to be in focus at one time. The SEM also produces images of high resolution, which means that closely spaced features can be examined at a high magnification. Preparation of the samples is relatively easy since most SEM one require the sample to be conductive.

The combination of higher magnification, larger depth of focus, greater resolution, and easy of sample observation marks the SEM one of the most heavily used instruments in research areas today.

2. TOXICOLOGICAL AND PHARMACOLOGICAL STUDIES

2.1 Experimental Animals

Wistar albino adult male rats weighing 200-350gm from animal housing facility of Vels University, were housed in polypropylene cages maintained with temperature 27°C ±1°C and 12 hrs light and dark cycles. The animals were allowed to acclimatize to the environment for one week and supplied with a standard pellet diet (Sai durga foods, Bangalore). The experimental protocol used in this study was approved by IAEC. (XIII/VELS/PCOL/10/2000/CPCSEA/IAEC/08.08.2012**).**

2.2 Acute Toxicity study

Acute oral toxicity was conducted as per the OECD guidelines 423-2001 (Acute Toxic Class Method) and Ecobichon (1997).

2.3 Screening the efficacy of Kadukkai Choornam on Triton induced hyperlipidemic rat

Procedure

Wistar rats weighing 200–350 g were starved for 18 h and then injected intravenously with 200 mg/kg Triton WR 1 339 (isooctyl-polyoxyethylene phenol). Serum cholesterol levels increase sharply 2–3 times after 24 h (phase I). The hypercholesterolemia decreases nearly to control levels within the next 24 h (phase II). The test drugs employed or the solvent for the controls are administered simultaneously with the Triton injection or 22 h thereafter. Serum cholesterol analyses are made 6, 24, and 48 h after Triton injection. The mechanism of the Tritoninduced hypercholesterolemia in phase I is thought to be due to increased hepatic synthesis of cholesterol through the ability of Triton to interfere with the uptake of plasma lipids by the tissues. Drugs interfering with cholesterol biosynthesis were shown to be active in phase I, while drugs interfering with cholesterol excretion and metabolism were active in phase II.

Experimental protocol

The animals were divided into five groups of six rats each. Group I served as normal control administered with 2% CMC only. Group II served as Hyperlipidemic Control administered with a single dose of triton 400 mg/kg. Group III and IV served as test groups received KC 250mg/kg and KC 500mg/kg respectively with triton administration. Group V served as standard treated with Lovastatin (10mg/kg/day) and Triton administration. All the animals after 72 hours of triton injection (ie. after inducing hyperlipidemia) the respective treatment was continued for 7 days.

Collection of blood

On the 8^{th} day the blood was collected by retro orbital sinus puncture, under mild ether anaesthesia. The collected samples were centrifuged for 10 minutes. Then serum samples were collected and it is used for various biochemical experiments. Then animals were sacrificed and collected the liver.

Liver lipid extraction

The liver was homogenized in cold 0.15M KCl and extracted with CHCl3: CH3OH (2% *v/v*). This lipid extract was used for the estimation of lipid parameters.

Biochemical analysis

The serum and liver were assayed total cholesterol, triglycerides, phospholipids, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL). The serum cholesterol levels were determined using semi auto analyser. The triglyceride, phospholipids, serum HDL, LDL and VLDL was calculated by using standard methods.

3. CLINICAL STUDY OF *KADUKKAI CHOORNAM*

3.1 Objectives

`The study was conducted on hyperlipidemic patients to assess the hypolipidemic activity of ***"KADUKKAI CHOORANAM"*** clinically, both in-patients and outpatients of both sex and varying age groups.

3.2 Study Centre

The clinical study for **HYPERLIPIDEMIA** is carried out in outpatient department and in patient ward of Govt.Siddha medical college hospital and Arignar Anna Indian Hospital, Arumbakkam, Chennai-106.

3.3 Design of the study:

Open clinical trial, phase II B

3.4 Selection:

50 patients from both sexes of various age groups were selected for clinical trial. Among 50 patients, 40 patients were treated as out-patients, 10 patients were treated as in– patients. The selection was based on the including and excluding criteria. They were clinically diagnosed on the basis of siddha principles with modern laboratory findings.

3.5 Registration Process

To register a patient, the following documents has been proceded.

- Copy of required laboratory tests
- Signed patient consent form then I verified eligibility and assigned a patient study number, drug dose and registered the patient on the study.

3.6 Selection Criteria:

Inclusion Criteria

- Sex: Both Male and female patient
- Age: 20 – 65 years
- BMI more than 25.
- Abdominal circumference more than 85 for females and more than 102 for males.
- Total cholesterol level more than 180mg/dl to 300 mg/dl, Triglycerides more than 150 mg%, LDL more than 100 mg%. Any one of the above parameter should be present to include in the trial.
- Patients who were willing to give consent

Exclusion Criteria

- Children, Pregnant women, elder subject more than 65 year
- Concurrent illness such as Diabetes mellitus type2, Nephrotic syndrome, Hypo thyroidism, Congestive cardiac failure, recent history of IHD
- Total cholesterol level more than 300 mg/dl

3.7 Criteria for withdrawal:

Patients were removed from study when any of the criteria listed below applies.In the absence of treatment delays due to adverse events, treatment may continue for 2 cycles or\ until one of the following criteria applies:

- Disease progression,
- Deterioration of vital signs with cardiac, respiratory, hepatic, renal and CNS changes.
- Intercurrent illness that prevents further administration of treatment,
- Unacceptable adverse event(s),
- Patient decides to withdraw from the study, or
- General or specific changes in the patient's condition render the patient unacceptable for further treatment in the judgment of the investigator.

3.8 Investigations:

For all the cases full clinical data were recorded and they were diagnosed on the basis of *SIDDHA* principles i.e. *Envagai Thrvugal*, *Ezhu Udal Thathukkal* etc. All the patients under study were subjected to blood investigations for TC, DC, ESR, Hb, Blood urea, Blood sugar .and lipid profile were done. Urine test for albumin, sugar, deposits and motion test for ova, cysts were done.

3.9 Routine examination and assessment

The full details of history and physical examination of the patients were recorded as per the proforma. The clinical assessment was done initially at the end of 7 days, 14 days and 21 days during treatment and at the end of the 21 days follow up were done. The laboratory investigation and the physiological parameters will be recorded initially and the end of the treatment and at follows up as per the Proforma.

3.10 Mode of administration of the test drug:

Form of the medicine : *Chooranam*

Route of Administration : Enteral

Dose : 1gm

Anubanam (Vehicle) : Warm water

Times of Administration : Two times a day; before food

Duration : 7 weeks

3.11 Diet and Medical Advice:

Do's

- Decrease portion size
- Decrease energy dense food
- Lot of vegetables
- Exercise
- Plenty of water

Dont's

- Fatty and tough meats
- Fried foods,
- Spicy foods, carbonated drink
- Snacking
- Day sleep

3.12 Trial Conduct:

This study will be conducted in compliance with the protocol approved by the Institutional Review Board, and according to Good Clinical Practice standards. No deviation from the protocol will be implemented without the prior review and approval of the IEC except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported to the IEC as soon as possible.

3.13 Criteria for assessment of response to therapy:

1) Marked response : 90% relief in the presenting signs and symptoms marked normality pathological investigation
2) Moderate response : 70 – 80% relief signs and symptoms, moderate normality of pathological investigation.
3) Mild response : 50% relief of signs and symptoms, mild changes in pathological investigations.
4) Poor response **:** less than 50% relief in symptoms and no significant improvement in laboratory parameters.

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3.14 **Ethical Review**

The protocol and amendments were submitted to the Govt siddha medical college, Institutional Ethical Committee (IEC) and got formal approval for conducting the study. The decision of the IEC concerning the conduct of the study was made in writing to the investigator.

All subjects for this study was provided a consent form describing this study and provided sufficient information for subjects to make an informed decision about their participation in this study. This consent form was submitted with the protocol for review and approval by the IEC. The formal consent of a subject, using the IEC-approved consent form, was obtained before that subject is submitted to any study procedure. This consent form was signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

Results & Discussion

CHAPTER IV

RESULTS AND DISCUSSION

Terminalia chebula, a kayakalpa drug which is compared to the mother for its efficacy was taken for its hypolipidemic activity. Here, various studies have been carried out in this study drug.

The study includes literary collections, Pharmacognostic study, physico and Phytochemicalanalysis, toxicological study, pharmacological study, and clinical study. The drug has been selected for the treatment of obesity in reference with Gunapadam mooligai vaguppu.

The prime action of Terminalia chebula is Rejuvenative. Botanical aspect of the fruit source shows the presence of tannins.Tanins act as a free radical scavenger and may prevent atherogenesas (Saravanan Subramanian et.al)the lateral research views emphasis antioxidant,antibacterial,antimutagenic properties of the drug

1. Pharmacognostic aspect of *Terminalia chebula*

1.1 Macroscopic characters (Fig 1)

The fruit is not winged. It is ovoid, faintly angled. Dry fruit is hard woody and it is indehiscent. Intact fruit yellowish-brown, ovoid, 20-35 mm long, 13-25 mm wide, wrinkled and ribbed longitudinally, pericarp fibrous, 3-4 mm thick, non-adherent to the seed, taste, astringent**.**

Figure 1: Dried Kadukkai fruit

1.2 Microscopic characters

In transverse sectioned view, the pericarp consists of a thin epidermal layer of thin cells. The cell walls of the epidermal cells are thick and have thick cuticle. The outer part of pericarp appears as thick dark hand which consist of thick peridermis zone. The peridermis includes five layers of this tabular cells. Inner to the periderm zone is another zone of larger rectangular cells which are arranged in more or less radial rows. Inner to the dark outer part of the pericarp is wide parenchymatous mesocarp. This inner mesocarp is a complex tissue system comprising outer thick layers of tangentially oriented thick walled lignified fibres. Next to the sclerotic layers is parenchymous part in which large and small vascular strands are scattered. Long irregular strands are seen spread over the mesocarp. Thus no well organized vascular bundles are recognized,inspite of abundance of vascular elements are present in the mesocarp. Diffusely distributed in the mesocarp parenchyma cells, these are prominent calcium oxalate druses. The druses occur in the unmodified parenchyma cells. The druses are solitary in the cells. The druses are 50µm thick.

Figure 2

Figure 3.1`

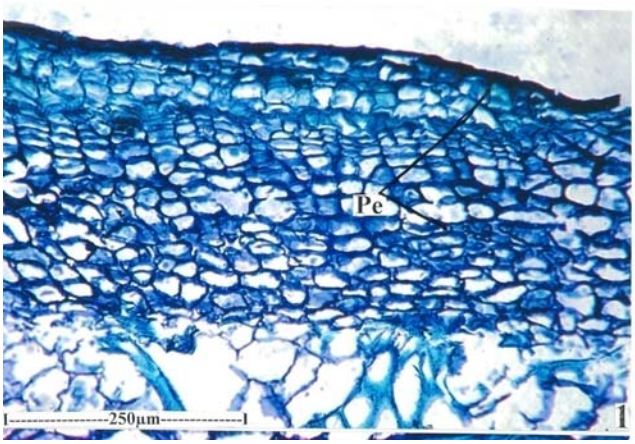
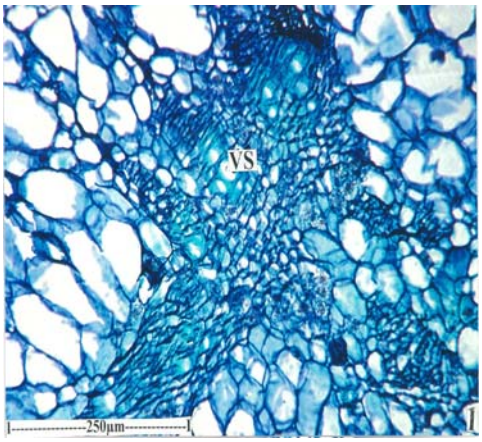


Figure 3.2



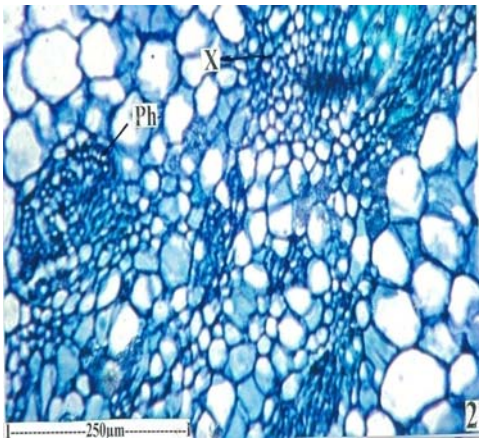


Figure 4.1

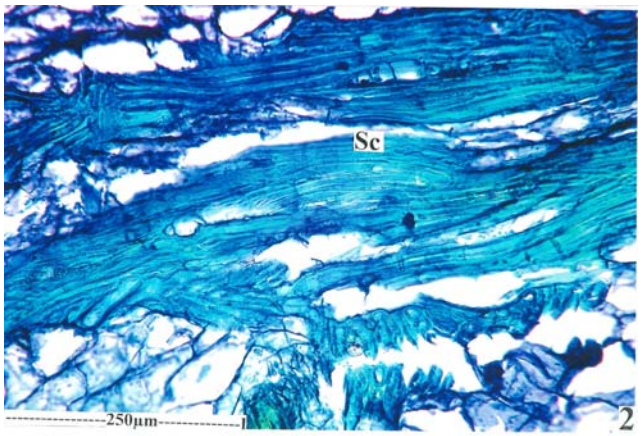
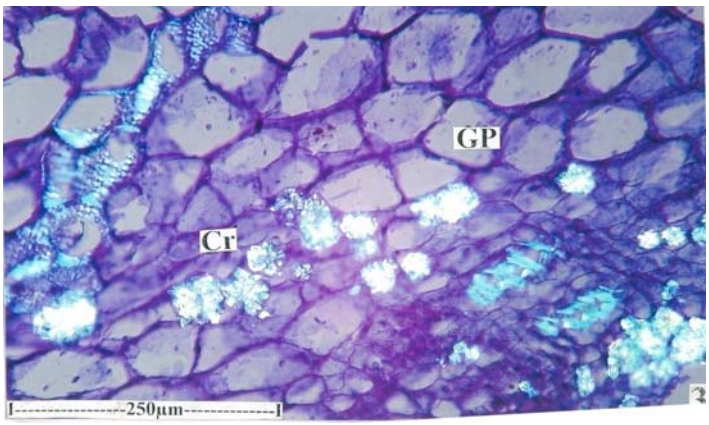


Figure 3.2



Legend for the above figures

Fig 2. T.S of- Pericarp, Entire view

(GP Ground Parenchyma, IPC Inner Pericarp, Outer Paricarp, SC Sclerenchyma ,VS Vascular Strand)

Fig.3.1. T.S of Pericarp Outer Zone Periderm

3.2.Outer Zone showing horizontal layers of sclerenchyma elements

Pe Periderm, SC Sclerenchyma

Fig 4.1 Vascular strands in the mesocarp

4.2.Calcium Oxalater Crystals in the mesocarp under polarized light

2. Finished form of *Kadukkai Choornam* (KC)

The KC was prepared following strictly the method mentioned in the Siddha text. The finished KC gave positive results to all tests for *Choornam* as mentioned in Siddha Gunapadam literature.

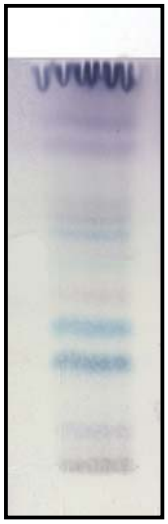
Figure 5: Kadukkai Choornam

3. PHYSICO-CHEMICAL ANALYSIS

Table 1: Physicochemical parameters

S.No	Parameter	Mean Value
1.	Loss on Drying at 105°C	5.3 %
2.	Total Ash	3.0 %
3.	Acid insoluble Ash	0.3 %
4.	Water Soluble Extractive	53.7 %
5.	Alcohol Soluble Extractive	59.6 %
6.	Particle size	Completely passes through sieve no.44
7.	pH	6.0

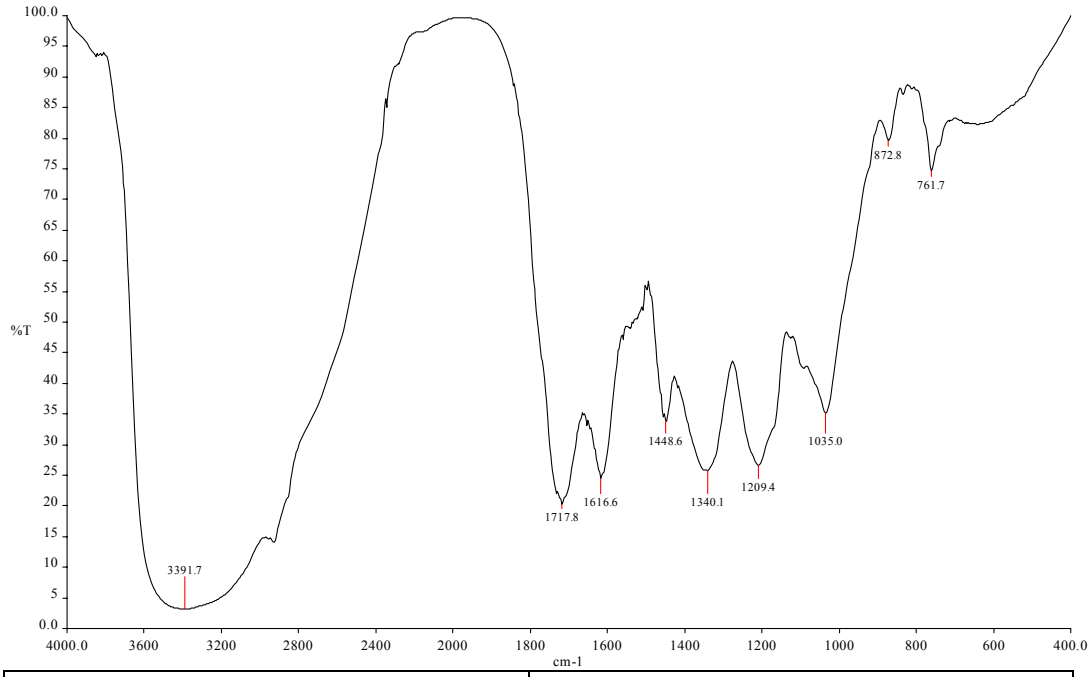
TLC analyses



After spray with visualizing agent

S.No	After Dipping in Vanillin-Sulphuric acid	
	Rf value	**Colour of the spot**
1	0.09	Grey
2	0.26	Blue
3	0.34	Blue
4	0.41	Grey
5	0.46	Blue
6	0.57	Blue
7	0.60	Purple
8	0.64	Grey
11	0.79	Purple
12	0.83	Purple

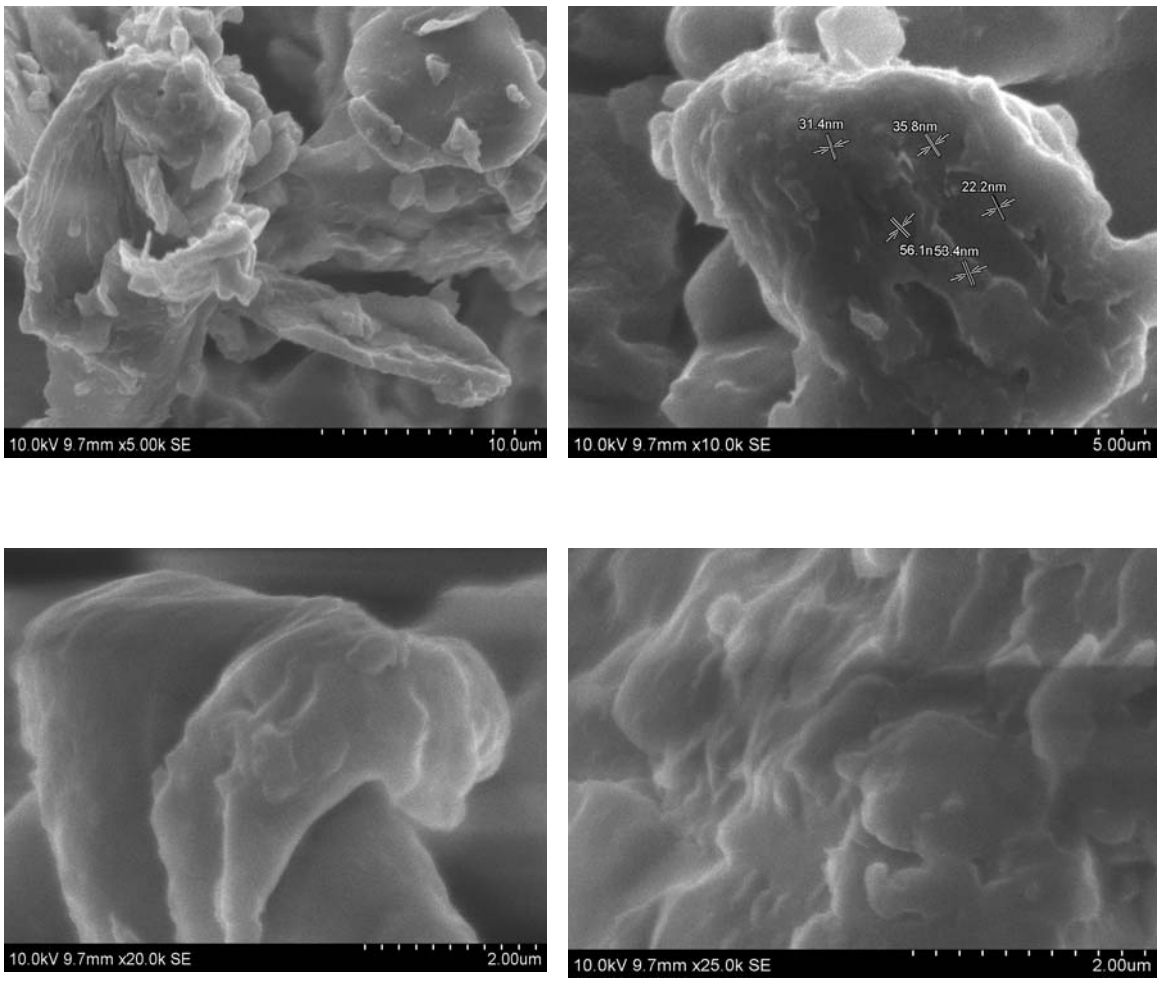
FTIR RESULTS



FREQUENCY BANDS	FUNCTIONAL GROUP
3391.7	ALCOHOL/PHENOL O-H STRETCH
1717.8	CARBOXYLIC ACID C=O STRETCH
1616.6	AROMATIC C=C BENDING
1448.6	
1340.1	ALKYL-METHYL
1209.4	
1035.0	FLUORO ALKANES- ORDINARY
872.8	AROMATIC- META DISUBSTITUTED BENZENE C-H
761.7	AROMATIC C-H BENDING

These bands indicate the presence of carboxylic acid, alkynes, and aromatic functional groups

SCANNING ELCTRON MICROSCOPE (SEM)



The above plates indicates that all the particles are in nano level. This particle size makes. the choornam for better absorption.

For drug delivery biodegradable nano particle formulations are needed as it is the intention to transport and release the drug in order to be effective.

TABLE 2: PHYTOCHEMICAL ANALYSIS OF *TERMINALIA CHEBULA*

Qualitative Phytochemical Tests		
1.	Alkaloids	Negative
2.	Triterpenes	Negative
3.	Tannin	Positive
4.	Flavonoids	Negative
5.	Steroids	Positive
6.	Glycoside	Positive
7.	Saponin	Positive
8.	Phenol	Positive

Phytochemical analysis revealed that Terminalia chebula contain **phenols,Tannin,Steroids,Saponin.**

The Tannin may act as in free radical scavenging mechanism and may prevent atherogenisis.Plant sterols may be interacted with the intestinal absorption of fats and cholesterols,it will promote the elimination of fats and cholesterol(Saravanan Subramanin et.al,2009)

Phenols inhibit the lipid peroxidation(Toko Yoshioko et.al,1989)

TABLE 3: PRELIMINARY CHEMICAL ANALYSIS OF *KADUKKAI CHOORNAM*

S.No.	EXPERIMENT	RESULT
1	Reducing sugar	-
2	Starch	-
3	Protein	-
4	Amino acid	-
5	Albumin	-
6	Phosphate	-
7	Sulphate	+
8	Chloride	+
9	Iron	+
10	Calcium	+
11	Sodium	-
12	Potassium	-
13	Zinc	-
14	Magnesium	-
15	Alkaloids	-
16	Tannic acid	+

From the preliminary chemical analysis,we came to know that the trial drug have Tannic acid,calcium,Iron,chloride and sulphate.

Calcium's ability to lower cholesterol has been known for several years. People who live in areas with hard water are known to have a lower incidence of death and complications from cardiovascular disease than those who drink soft water, and it is believed that calcium may have something to do with this.

It is thought to work by binding to bile acids and cholesterol in the small intestine, similar to the way fiber and bile acid resins work. By binding to cholesterol in the small intestine,

Cholesterol is not absorbed into the blood and is instead excreted out of the body in the feces.(By Jennifer Moll, About.com Guide (*Updated October 08, 2008)*

Calcium can enhance the reduction of serum cholesterol in pigs that had been fed a high cholesterol diet, probably through alteration in the enterohepatic circulation of bile acids.(B.Z.De Rodes et.al,Dec 1996)

Iron deficiency enhances cholesterol gallstone formation

an iron-deficient diet (1) alters hepatic enzyme metabolism, which, in turn, (2) increases gallbladder bile cholesterol and promotes cholesterol crystal formation (SeahM Johnston et.al,Aug 1997)

4. TOXICOLOGICAL AND PHARMACOLOGICAL STUDIES

4.1 ACUTE TOXICITY PROFILE

Based on the results pooled from the acute toxicity study the therapeutic dose was fixed as 250 and 500mg/kg in this study since the drug is pharmacologically safe. Hyperlipidemia is associated with the heart diseases, which is the leading cause of death in the world. The results were discussed as Lipid profile in serum and Lipid profile in liver. LDL and VLDL levels were significantly increased in triton injected animals compared to normal control. Lipid profile in serum and liver indicates the increased phospholipids; triglyceride and cholesterol levels were significantly reduced by treatment of 250 and 500 mg kg-1 of Kadukkai Chooranam.

The decrease in cholesterol may indicate increased oxidation of mobilized fatty acids of inhibition or lipolysis. The present investigation shows that all triton induced rats displayed hyperlipidemia as shown by their elevated levels of serum and liver cholesterol, triglyceride, VLDL, LDL and also the reduction in the HDL level. Literature reveals that an increase in HDL cholesterol and decrease in TC, LDL cholesterol and TG is associated with a decrease in the risk of ischemic heart diseases.

4.2 EFFICACY STUDY AGAINST HYPERLIPEMIA ON RAT

In general, hyperlipidemia was classified into primary and a secondary type clearly indicates the complexities associated with disease. Consumption of more fat may lead to the production of increased VLDL, resulting in the formation of maximum amounts of LDL which may stick to the walls of the blood vessels causing blockages for the normal flow of blood.

Triton Wr-1339 has been widely used to block clearance of triglyceride-rich lipoproteins to induce acute hyperlipidemia particularly, in rats it has been used for screening natural or chemical hypolipidemic drugs. The results shows that Kadukkai Chooranam produced a significant reduction in cholesterol level and also it reversed Triton induced hypolipidemic in rats. Similarly, Kadukkai Chooranam at a dose of 250 and 500mg/kg significantly lowered both plasma triglycerides and cholesterol levels. The reduction of total cholesterol by the Kadukkai Chooranam at the dose level of 250 and 500 mg kg-1 may be associated with a decrease of LDL, which is the ultimate aim of many hypolipidemic agents.

This study suggests that cholesterol-lowering activity of the Kadukkai Chooranam also may result from the catalytic action on LDL cholesterol for final elimination in the form of bile acids. Abnormalities in cellular cholesterol metabolism could partly be responsible for the changes in the plasma cholesterol levels in diabetes. Diabetes is also associated with hyperlipidemia. Serum total cholesterol and triglycerides have been decreased significantly in diabetic rats after *Kadukkai Chooranam* administration. These effects may be due to low activity of cholesterol biosynthesis enzymes or low-level lipolysis that is under the control of insulin. The *Kadukkai Chooranam* treatment also resulted in significantly reverted the level of LDL and HDL in serum towards the normal, which again confirms the hypolipidemic effect.

It can be concluded that *Kadukkai Chooranam* 250 and 500 mg kg-1 treatment was effective in cholesterol, TG, VLDL, LDL and HDL. The antihyperlipidemic activity of *Kadukkai Chooranam* against Triton Wr-1339 showed dose dependent activity when compared to control as well as Lovastatin treated groups. Thus, our study showed that administration of *Kadukkai Chooranam* of both 250 and 500 mg kg-1 dose was effective to treat hyperlipidemia.

Table 4: Effect *of Kadukkai Chooranam* on body weight of Triton-induced hyperlipidemic rats

Groups	Body Weight (gm.)				
	Initial	1st Week	2nd Week	3rd Week	4th Week
Normal control	154.28±2.73	156.18±2.35	158.12±2.44 **	161.22±2.92 **	163.46±3.00 **
Hyperlipidemic Control	156.24±2.54	156.99±2.71	178.22±2.60	196.84±2.48	236.13±2.75
KC 250mg/kg	153.88±2.00	157.04±2.36	166.79±2.48 *	182.40±3.22 **	180.11±2.44 **
KC 500mg/kg	156.62±2.26	159.00±2.44	166.15±2.56 *	180.12±2.82 **	186.18±2.52 **
Lovastatin (10mg/kg/day)	155.18±2.11	158.27±2.68	165.92±2.88 **	179.37±2.46 **	180.40±2.11 **

Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

Table 5: Effect of *Kadukkai Chooranam* on Blood lipid profile of Triton-induced hyperlipidemic rats.

Group	Treatment	T.C.	T.G.	LDL	HDL	VLDL
I	**Normal Control**	70.12±2.15**	66.32±2.01**	50.04±1.37**	35.036±8.40	18.02±0.24**
II	**Triton Control**	174.75±1.452	126.77±18.50	122.10±3.34	28.15±0.52	25.71±3.02
III	**KC 250mg/kg**	68.45±1.767**	73.62±9.56**	70.17±10.41**	94.51±16.433**	14.30±1.29**
IV	**KC 500mg/kg**	73.46±2.107**	56.95±1.152**	55.12±6.745**	50.12±8.15	11.15±0.32**
V	**Lovastatin (10mg/kg/day)**	55.58±4.78**	53.15±10.04**	46.40±6.14**	52.50±14.14	10.51±2.04**

Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

Table 6: Effect of *Kadukkai Chooranam* on liver lipid profile of Triton-induced hyperlipidemic rats.

Group	Treatment	T.C.	T.G.	LDL	HDL	VLDL
I	**Normal Control**	74.36±7.28**	70.62±4.282**	26.182±1.114**	36.158±10.62	14.126±0.775**
II	**Triton Control**	155.41±10.44	178.112±15.212	105.41±4.20	18.040±1.26	35.755±4.025
III	**KC 250mg/kg**	75.22±6.248**	65.424±3.500**	18.14±5.002**	44.15±3.320	12.125±0.712**
IV	**KC 500mg/kg**	82.7±6.952**	59.255±2.092**	23.10±5.140**	50.455±12.024*	12.52±0.274**
V	**Lovastatin (10mg/kg/day)**	67.754±5.125**	87.647±7.104**	20.28±5.403**	36.74±6.502	12.11±1.459**

Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

Table 7: Effect of Kadukkai Chooranam on atherogenic index and percentage protection of different groups.

Groups	Atherogenic Index	% Protection
Normal control	2.38±0.16	----
Hyperlipidemic Control	4.65±0.22	----
KC 250mg/kg	3.48±0.04	25.16
KC 500mg/kg	3.11±0.04	33.11
Lovastatin (10mg/kg/day)	2.86±0.06	38.49

Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

Table 8: Effect of Kadukkai Chooranam on SGOT, SGPT Total protein, Urea and Blood glucose levels of Triton-induced hyperlipidemic rats

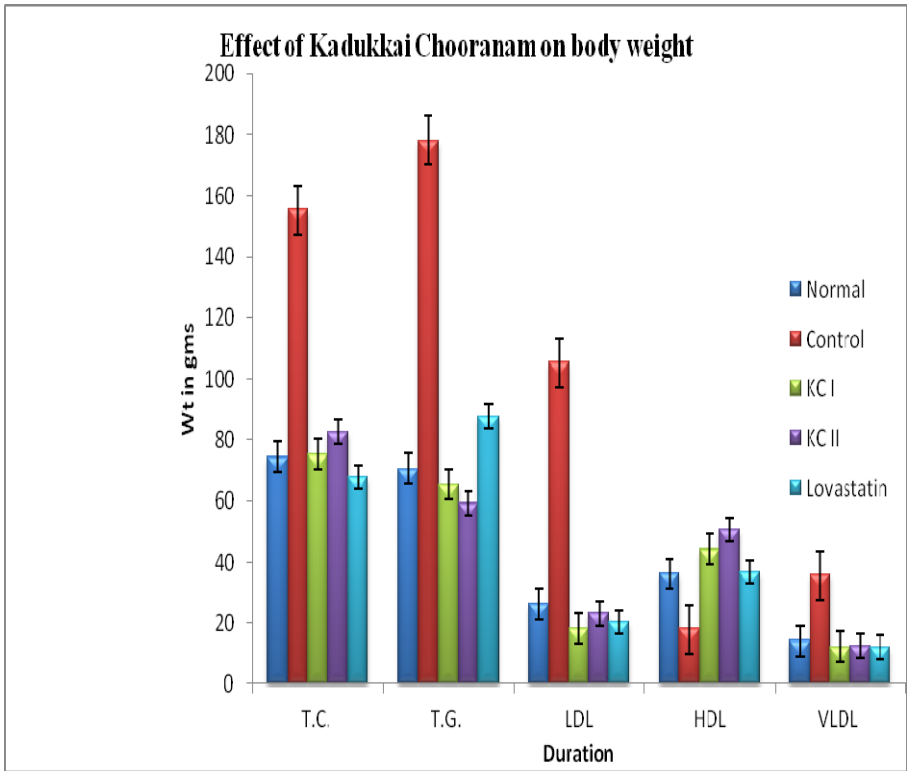
Groups	SGOT(IU/L)	SGPT(IU/L)	Total Protein (gm/dl)	Urea (mg/dl)	Blood Glucose (mg/dl)
Normal control	168.18±4.70**	61.12±2.72**	5.95±0.31*	42.04±0.92**	84.84±1.50**
Hyperlipidemic Control	230.48±5.42	130.42±4.51	7.22±0.30	26.11±0.98	93.56±1.82
KC 250mg/kg	157.80±5.71**	64.18±2.31**	6.10±0.30*	34.08±2.10*	85.11±1.30**
KC 500mg/kg	196.48±5.48**	101.04±2.64**	6.98±0.28	40.64±2.45**	83.10±1.14**
Lovastatin (10mg/kg/day)	170.14±5.60**	72.46±2.87**	6.23±0.31	36.98±2.00**	82.34±1.12**

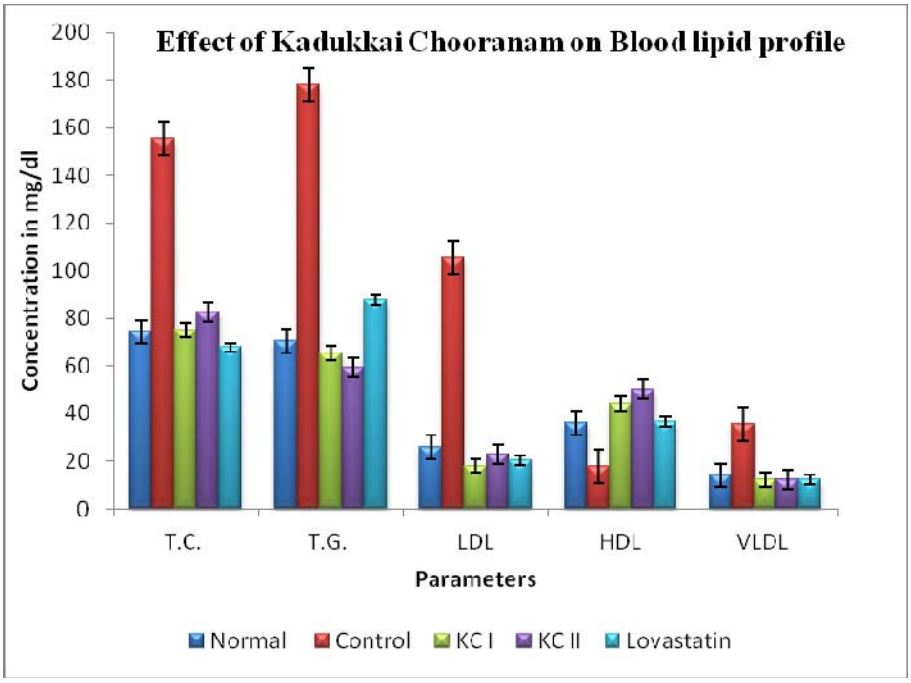
Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

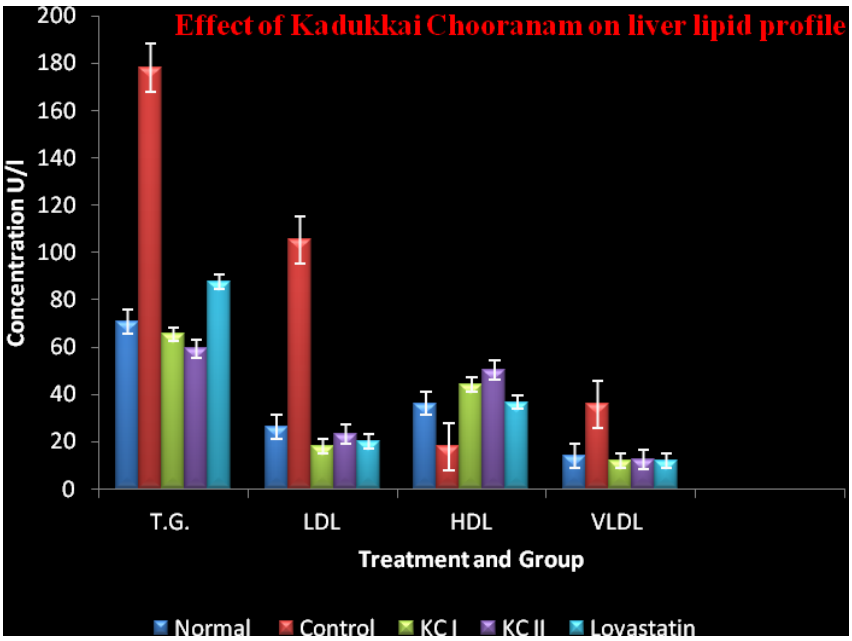
Table 9: Effect of Kadukkai Chooranam on vital organ weights of Triton-induced hyperlipidemic rats on day 24.

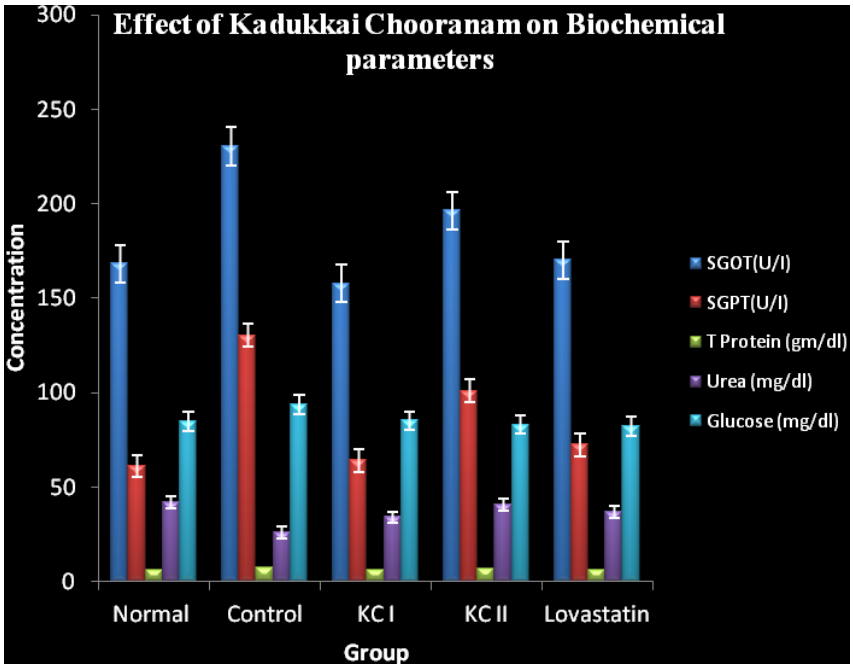
Groups	Liver(gm)	Heart(gm)	Kidney(gm)
Normal control	5.45±0.28**	0.61±0.05**	0.55±0.18
Hyperlipidemic Control	7.88±0.17	1.02±0.05	0.84±0.03
KC 250mg/kg	5.82±0.15**	0.58±0.10**	0.58±0.02
KC 500mg/kg	6.61±0.3**	0.64±0.02**	0.64±0.03
Lovastatin (10mg/kg/day)	5.92±0.03**	0.62±0.02**	0.60±0.14

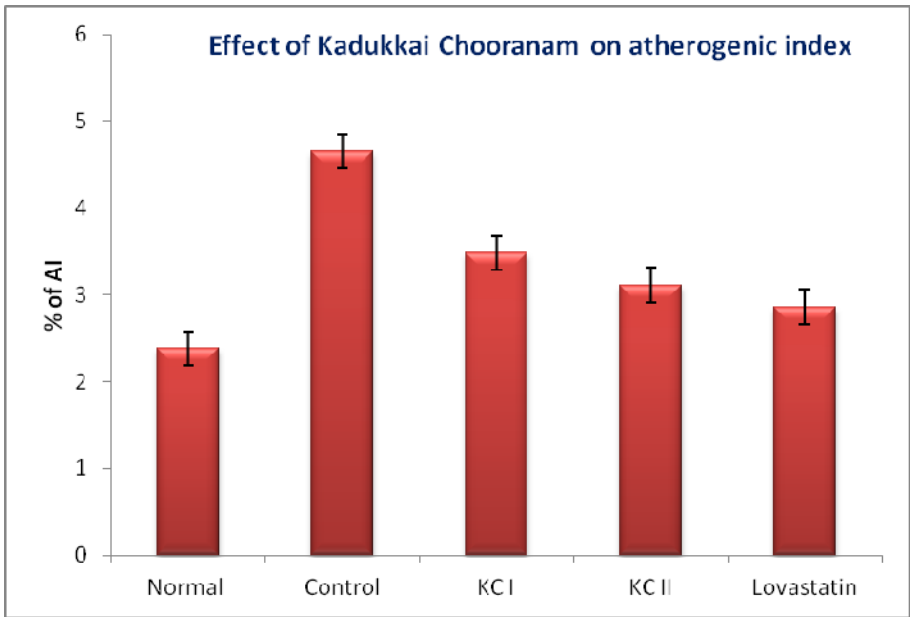
Values are as mean ± SEM (n=6)
Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001
Comparison made between Group II Vs Group I
Group III, IV, V Vs Group II.

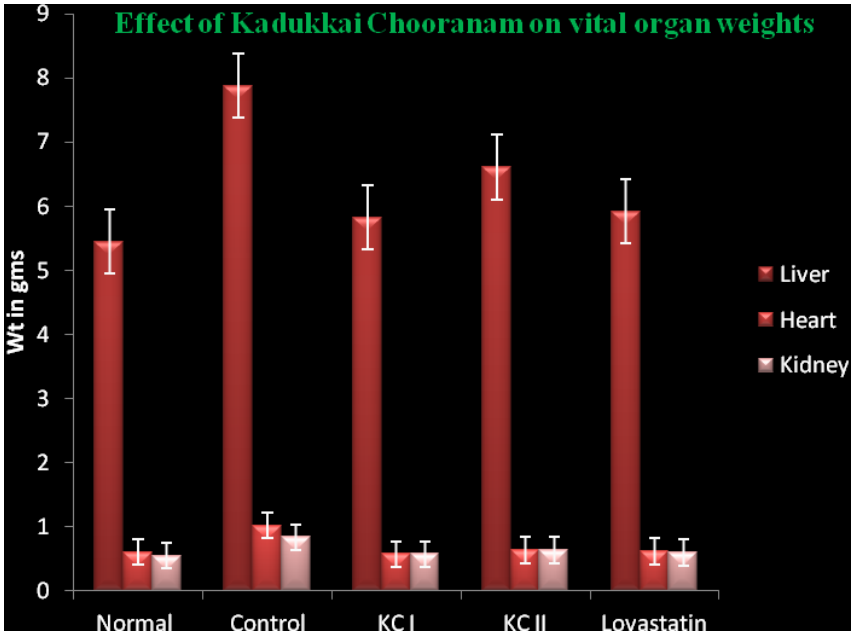

Effect of Kadukkai Chooranam on body weight
Wt in gms
200
180
160
140
120
100
80
60
40
20
0
T.C.
T.G.
LDL
HDL
VLDL
Duration
Normal
Control
KC I
KC II
Lovastatin


Effect of Kadukkai Chooranam on Blood lipid profile
Concentration in mg/dl
200
180
160
140
120
100
80
60
40
20
0
T.C.
T.G.
LDL
HDL
VLDL
Parameters
Normal
Control
KC I
KC II
Lovastatin


Effect of Kadukkai Chooranam on liver lipid profile
Concentration U/l
200
180
160
140
120
100
80
60
40
20
0
T.G.
LDL
HDL
VLDL
Treatment and Group
Normal
Control
KC I
KC II
Lovastatin


Effect of Kadukkai Chooranam on Biochemical parameters
Concentration
300
250
200
150
100
50
0
Normal
Control
KC I
KC II
Lovastatin
Group
SGOT(U/l)
SGPT(U/l)
T Protein (gm/dl)
Urea (mg/dl)
Glucose (mg/dl)


Effect of Kadukkai Chooranam on atherogenic index
% of AI
0
1
2
3
4
5
6
Normal
Control
KC I
KC II
Lovastatin

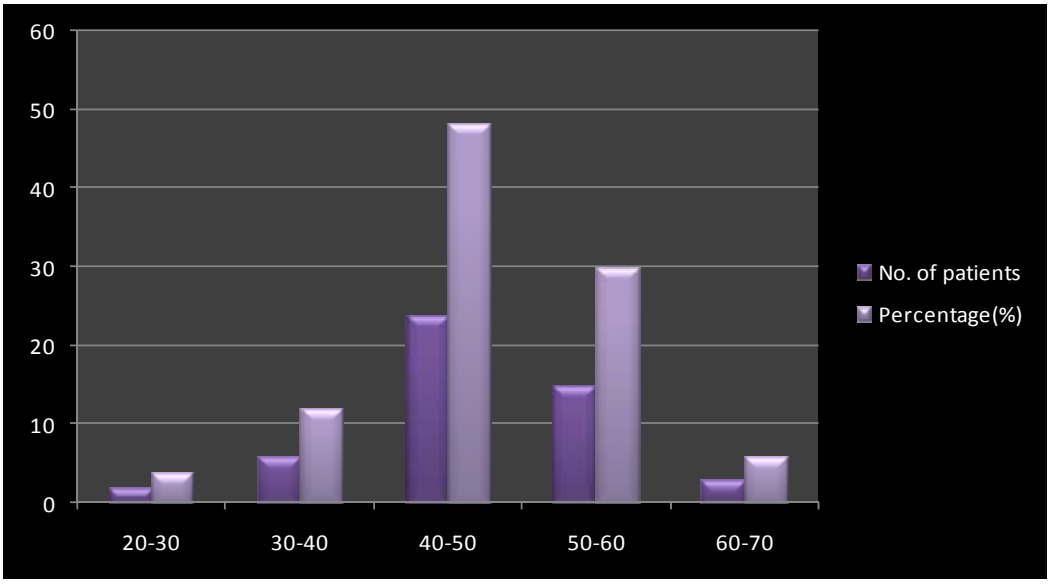

Effect of Kadukkai Chooranam on vital organ weights
Wt in gms
0
1
2
3
4
5
6
7
8
9
Liver
Heart
Kidney
Normal
Control
KC I
KC II
Lovastatin

5. CLINICAL ASSESMENT

Hyperlipidemia is typically due to a combination of environmental and genetic factors include obesity and dietary choices. A number of secondary causes including Diabetes mellitus type2, nephrotic syndrome, hypo thyroidism etc. Even though there is a lot of medications available for this disease, still there is a thrive for less adverse effect drugs. Herbal medicines are playing vital role on curing diseases without marked adverse effects even though on long term intake. From this plant kingdom I have selected this herb which proved its hypolipdemic activity preclinically. *Kadukkai chooranam*, a herbal medicine was used for this clinical trial to prove its safety and efficacy against hyperlipidemia.

Age wise distribution

S.No.	Age in years	No.of patients	Percentage(%)
1	20-30	2	4
2	30-40	6	12
3	40-50	24	48
4	50-60	15	30
5	60-70	3	6
Total		50	100



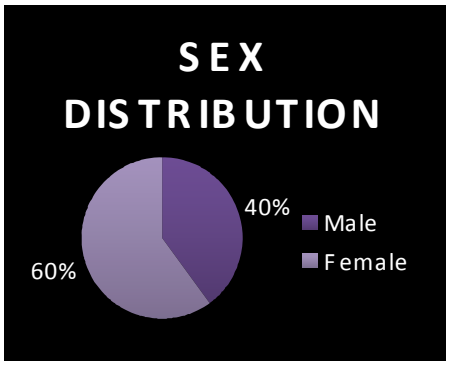
INFERENCE:

Among 50 patients,

- 2 patients are between 20 to 30 yrs.
- 6 patients are between 30 to 40 yrs.
- 24 patients are between 40 to 50 yrs.
- 15 patients are between 50 to 60 yrs
- 3 patients are between 60 to 70 yrs

SEX DISTRIBUTION

S.NO	SEX	NO.OF PATIENTS	PERCENTAGE
1	MALE	20	40%
2	FEMALE	30	60%
Total		50	100%



INFERENCE:

Among 50 patients,30 people are female and 20 people are male.

Clinical study on kadukkai choornam in the management of hyperlipidaemia .

S.no	OP no.	NAME, AGE/SEX	COMPLAINTS	DURATION OF DAYS (TREATMENT)	BT + AT	INVESTIGATION					RESULT
						LIPID PROFILE					
						TOTAL CHOLESTROL mg/dl	TRIGLYCERIDES Mg/dl	HDL Mg/dl	LDL Mg/dl	VLDL mg/dl	
1	3574	MEENAKSHI, 58/F	Increase in weight, dyspnea	9.7.12 to 25.8.12	BT	222.4	128	47.2	149.2	25.6	Marked
					AT	190	120	50.2	110	25	
2	3584	SARASWATHI, 57/F	Increase in weight, dyspnea, tiredness	9.7.12 to 24.8.12	BT	240	120	30	139.6	30.4	
					AT	195	110	45	100	30	Marked
3	5963	VATSALA, 56/F	Increase in weight,tiredness	17.7.12 to 25.8.12	BT	190	160	30	110	45	
					AT	170	100	47.4	90	35	Moderate
4	8659	RAMALINGAM,60/M	Increase in weight,tiredness	28.7.12 to 5.9.12	BT	210	140	30	140	30	
					AT	180	120	50	90	25	Marked
5	8702	DANALAKSHMI,50/F	Increase in weight,tiredness	28.7.12 to 4.9.12	BT	224	128	30	152	45	
					AT	190	120	45	137	25	Marked
6	1655	MANONMANI,45/F	Increase in weight,tiredness	9.8.12 to 19.9.12	BT	197.6	97	30	140	20	
					AT	150	90	50	100	18	Mild
7	1712	SELVI,45/F	Increase in weight,tiredness	9.8.12 to 20.9.12	BT	218	126	25	147	25.6	
					AT	200	120	50	98	22.7	Marked
8	3567	INDHIRANI,52/F	Increase in weight,tiredness	17.8.12 to 29.9.12	BT	250	120	30	139	40	
					AT	200	90	46	98	35	Marked

9	4282	DEEPA, 24/F	Increase in weight,tiredness	21.8.12 to 30.9.12	BT	210	130	30	140	37	
					AT	190	100	45	120	30	Moderate
10	2759	SHYMALA,29/F	Increase in weight,tiredness	26.9.12 to 30.10.12	BT	242	120	25	150	30	
					AT	190	100	45	100	25	Marked
11	7308	MOHAN,56/M	Increase in weight,tiredness	15.10.12 to 25.11.12	BT	270	130	30	140	40	
					AT	220	120	50	90	37	Marked
12	8858	SHANTI,40/F	Increase in weight,tiredness	23.10.12 to 30.11.12	BT	250	170	27	140	38	
					AT	200	150	40	120	30	Marked
13	9207	SRIDARAN,60/M	Increase in weight,tiredness	25.10.12 to 30.11.12	BT	240	150	35	150	35	
					AT	190	120	48	100	32	Marked
14	9225	LATHA,35/F	Increase in weight,tiredness	25.10.12 to 29.11.12	BT	250	150	35	110	40	
					AT	210	130	47	75	37	Marked
15	981	HEMALATHA,45/F	Increase in weight,tiredness	3.11.12 to 14.12.12	BT	260	140	30	110	40	
					AT	200	120	46	78	38	Marked
16	1398	KUMAR,40/M	Increase in weight,tiredness	5.11.12 to 16.12.12	BT	240	150	30	100	32	
					AT	190	90	48	75	30	Marked
17	1524	ARUNPUZHAVI,38/F	Increase in weight,tiredness	6.11.12 to 24.12.12	BT	220	140	33	110	32	
					AT	190	120	44	72	28	Marked
18	1665	RADHIKA, 45/F	Increase in weight,tiredness	6.11.12 to 28.12.12	BT	197	134	32	150	29	
					AT	177	123	45	100	25	Marked
19	2086	RAJAN,58/M	Increase in weight,tiredness	8.11.12 to 20.12.12	BT	270	156	32	124	33	

					AT	229	129	42	93	29	Marked
20	2163	GEETHA,45/F	Increase in weight,tiredness	8.11.12 to 18.12.12	BT	224	144	33	120	42	
					AT	187	124	47	91	32	Marked
21	2533	MAHALINGM,46/M	Increase in weight,tiredness	10.11.12 to 24.12.12	BT	217	152	32	110	36	
					AT	191	132	50	76	28	Marked
22	5055	THAMIZHSELVI,35/F	Increase in weight,tiredness	22.11.12 to 29.12.12	BT	256	150	34	93	40	
					AT	201	120	52	78	28	Marked
23	5836	VAISHNAVI,35/F	Increase in weight,tiredness	26.11.12 to 30.12.12	BT	240	146	36	111	35	
					AT	197	126	54	98	32	Marked
24	5832	KALYANI, 35/F	Increase in weight,tiredness	26.11.12 to 31.12.12	BT	190	132	31	139	40	
					AT	170	123	46	100	30	Marked
25	5596	VELAMMAL,43/F	Increase in weight,tiredness	24.11.12 to 28.12.12	BT	240	150	35	112	43	
					AT	211	110	51	89	31	Marked
26	5579	GEETHA, 35/F	Increase in weight,tiredness	24.11.12 to 29.11.12	BT	228	150	38	109	36	
					AT	197	110	53	89	30	Marked
27	5577	THYAGU, 43/M	Increase in weight,tiredness	24.11.12 to 31.12.12	BT	220	160	33	120	44	
					AT	190	110	58	90	32	Marked
28	5578	MARIYAPPAN,44/M	Increase in weight,tiredness	24.11.12 to 2.1.13	BT	234	150	28	110	37	
					AT	198	110	42	90	31	Marked
29	5612	NAGAMANI,57/M	Increase in weight,tiredness	25.11.12to31.12.12	BT	217	160	32	118	32	
					AT	198	120	47	97	28	Moderate
30	5634	SARASU,48/F	Increase in weight,tiredness	25.11.12to 2.1.13	BT	260	158	34	120	43	

					AT	190	110	52	90	33	Marked
31	5645	PULAVENTHAN,42/M	Increase in weight,tiredness	26.11.12to 29.12.12	BT	258	158	43	120	40	
					AT	210	110	53	90	35	Marked
32	5676	JEBA,49/F	Increase in weight,tiredness	26.11.12to 30.12.12	BT	280	170	35	120	33	
					AT	210	120	52	95	27	Moderate
33	5693	ALAMELU,60/F	Increase in weight,tiredness	27.11.12to 31.12.12	BT	290	158	35	110	40	
					AT	200	126	55	98	30.5	Marked
34	5732	RAMANI,47/F	Increase in weight,tiredness	27.11.12to 31.12.12	BT	234	150	25	128	38	
					AT	194	115	43	97	30	Marked
35	5743	JAGA,45/F	Increase in weight,tiredness	28.11.12to 3.1.13	BT	297	158	40	100	40	
					AT	220	110	50	87	33	Moderate
36	5756	NEELA,46/F	Increase in weight,tiredness	28.11.12to 2.1.13	BT	257	157	35	120	35	
					AT	200	120	53	83	25	Marked
37	5764	RANI,40/F	Increase in weight,tiredness	28.11.12to 31.12.12	BT	233	187	43	160	34	
					AT	187	112	55	104	23	Marked
38	5832	PREETHI,54/F	Increase in weight,tiredness	29.11.12to 3.1.13	BT	212	157	37	109	43	
					AT	184	104	48	97	22	Marked
39	5856	SATHIYA 45/F	Increase in weight,tiredness	29.11.12to 2.1.13	BT	287	157	32	110	43	
					AT	217	112	48	97	22	Marked
40	5898	GAYATHRI,56/F	Increase in weight,tiredness	30.11.12to 2.1.13	BT	270	170	35	97	40	
					AT	210	113	50	83	35	Marked

S.no	IP no.	NAME, AGE/SEX	COMPLAINTS	DURATION OF DAYS (TREATMENT)	BT + AT	INVESTIGATION					RESULT
						LIPID PROFILE					
						TOTAL CHOLESTROL mg/dl	TRIGLYCERIDES Mg/dl	HDL Mg/dl	LDL Mg/dl	VLDL mg/dl	
1	1184/9933	ANTHONI,41/M	Increase in weight, dyspnea	2.8.12 to 17.8.12	BT	223.4	129	47.2	149.2	25.6	Marked
					AT	188	119	52.2	110	25	
2	1298/3358	KANNUSMY,52/M	Increase in weight, dyspnea, tiredness	17.8.12 to 28.8.18	BT	243	122	32	139.6	30.4	
					AT	195	113	43	102	30	Marked
3	1369/5885	JAGADESAM,45/M	Increase in weight,tiredness	28.8.12 to 10.9.2	BT	191	161	36	117	45.7	
					AT	174	103	47.4	93	35	Moderate
4	1381/6083	ROOPASEKAR,58/M	Increase in weight,tiredness	30.8.12 to 11.9.12	BT	213	144	32	143	30.4	
					AT	184	113	52	90.6	24	Marked
5	1414/7122	VELU,47/M	Increase in weight,tiredness	3.9.12 to 29.9.12	BT	227	123	32.7	153	43	
					AT	195	118	41	137.5	27	Marked
6	315/9287	RAMESH KUMAR, 55/M	Increase in weight,tiredness	25.10.12 to 9.11.12	BT	197.6	96	30.3	140.8	22	
					AT	154	87	50.1	103	18	Mild
7	449/4253	NARAYANAN,40/M	Increase in weight,tiredness	19.11.12 to 8.12.12	BT	218	196	24	147.8	25.6	
					AT	206	121	52	98.5	22.7	Marked
8	586/8275	NAGARAJ,54/M	Increase in weight,tiredness	6.12.12 to 17.12.12	BT	251	122	34.8	139	44	
					AT	207	91	43	98	35	Marked
9	480/4811	SHANKAR,55/M	Increase in weight,tiredness	21.11.12 to 9.12.12	BT	213	133	32	143	37	
					AT	192	108	43	121	31	Moderate
10	553/6855	PERIYANNA,25/M	Increase in weight,tiredness	30.11.12 to 19.12.12	BT	242	123	23	154	30.4	

BMI RESULTS BEFORE AND AFTER ADMINISTRATION OF *KADUKKAI CHOORNAM*

S.no	OP/IP no.	NAME	AGE/SEX	BMI	
				BEFORE TREATMENT	AFTER TREATMENT
1.	3574	MEENAKSHI	58/F	29.7	27.5
2.	707	SARASWATHY	57/F	31	29
3.	5963	VATCHANA	56/F	29.4	28.4
4.	8659	RAMALINGAM	60/M	33.2	31.2
5.	8702	THANA LAKSHMI	50/F	28.5	26.5
6.	1655	MANOMANI	45/F	30.4	27.8
7.	1712	SELVI	45/F	36.8	34
8.	3567	INDIRARANI	52/F	31.6	30
9.	4282	DEEPA	24/F	32	30.1
10	2759	SHIYAMALA	29/F	30	28
11	7308	MOHAN	56/M	29.1	27.2
12	8858	SHANTI	40/F	31.1	29.4
13	9207	SRIDHARAN	60/M	32	30.8
14	9225	LATHA	35/F	32.6	29.7
15	981	HEMALATHA	45/F	32.87	30.5
16	1398	KUMAR	40/M	29.7	27.3
17	1524	ARULKUZHAVI	38/F	31.1	30
18	1665	RADHIKA	45/F	28.9	29.7
19	2086	RAJAN	58/M	29.67	26.2
20	2163	GEETHA	45/F	31.45	29.65
21	2533	MAHALINGAM	46/M	29.43	26
22	5055	THAMIZHSELVI	30/F	30	28.6
23	5836	VAISHNAVI	35/F	29.4	27.2
24	5832	KALYANI	35/F	30	29.1
25	5596	VELAMMAL	43/F	32.1	29
26	5579	GEETHA	35/F	33.2	31.9
27	5577	THIYAGU	43/M	31	28.7
28	5578	MARIAPPAN	44/M	29.8	27
29	5612	NAGAMANI	57/M	31.3	29.4
30	5634	SARASU	48/F	32	30.7

31	5645	PULAVENTHAN	42/M	29.9	27
32	5676	JEBA	49/F	31.5	29.1
33	5693	ALAMELU	60/F	30	27
34	5732	RAMANI	47/F	29.9	26.8
35	5743	JEGAN	45/F	33.4	31.8
36	5756	NEELA	46/F	32	29.2
37	5764	RANI	40/F	31.8	28
38	5832	PREETHI	54/F	29	27.2
39	5856	SATHYA	45/F	32.8	31
40	5898	GAYATHRI	56/F	29	27.7
41	1184/9933	ANTHONI	41/M	32	30
42	1298/3358	KANNUSAMY	52/M	32	31.1
43	1369/5885	JAGADESAN	45/M	31.4	28.6
44	1381/6083	ROOPASEKAR	58/M	33	31.6
45	1414/7122	VELU	47/M	29.3	25.9
46	3115/9287	RAMESH KUMAR	55/M	33	31
47	449/4253	NARAYANAN	40/M	30.3	27
48	586/8275	NAGARAJ	54/M	31.2	29
49	281/8609	GUNA SEKARAN	50/M	29	26
50	398/3173	KANNAMANI	58/M	30	29.1

Table no:10 **GRADATION RESULT**

S.NO	**LEVEL OF IMPROVEMENT**	**NO.OF .PATIENTS**	**PERCENTAGE (%)**
1	**Marked Response**	**40**	**80**
2	**Moderate Response**	**7**	**14**
3	**Mild Response**	**2**	**4**
4	**Poor Response**	**1**	**2**
	Total	**50**	**100**

INFERENCE

Among 50 patients

Marked response seen in 40 patients (80%)

Moderate response seen in 7 patients(14%)

Mild response in 2 patients (4%)

Poor response seen in 1 patient(2%)

Thus clinical study of kadukkai choornam on dyslipidemic patients showed a good result.

SUMMARY

The plant of *Terminalia chebula* (*Kadukkai*) had been collected from Kollimallai Hills, Salem district, Tamilnadu and authenticated by experts.

The literary review in *Siddha* and botanical aspects had been visibly discussed.

The drug was subjected to step wise process of investigations like pharmacognostic study phytochemical, chemical and physio-chemical analysis to report the creditability of drug.

From the preliminary chemical analysis,we came to know that the trial drug have Tannic acid,calcium,Iron,chloride and sulphate.Recent researches suggest the lipid lowering activity of Tannic acid,calcium,and iron.

Phytochemical analysis revealed the presence of tannins,phenols,sterods. Recent studies shows phenols inhibit the lipid peroxidation and Tannin may prevent atherogenesis.

Toxicity studies had its special role in placement of drug at its next level by establishment as safety drug.

Hypolipiemic activity was monitored through Body weight,BMI and waist circumference along with lipid profile. The clinical study had shown good improvement in patients.

As a result of scrutinisation of all results the unique *Siddha* medicine, powdered form of of *Terminalia chebula* (*Kadukkai chooranam*) will be significantly safe and highly effective.

CONCLUSION

The trial drug *Kadukkai chooranam* reveals the beneficial activity in reducing lipid levels

The model and study design demonstrates the feasibility of evaluating powdered form of *Terminalia chebula* (*Kadukkai chooranam*) in the management of hyperlipidemia.

The literary reviews along with phytochemical, chemical constituent's aids in justification of drug.Standardisation of drug through various physio chemical analysis and pharmacognostic study had emerged as a part of study for quality and acceptability of drug.

The availability, collection and preparation of the drug is simple. Acute toxicity studies in animals had revealed the safety of the drug .

Pharmacological study suggests that cholesterol-lowering activity of the Kadukkai Chooranam may result from the catalytic action on LDL cholesterol for final elimination in the form of bile acids.

The clinical trial shows the possible benefits of the drug in treating hyperlipidemia with 80% marked response, 7% moderate response with increasing HDL level and decreasing LDL levels

The study justifies the magnitude of *Terminalia chebula* (*Kadukkai chooranam*) for lowering cholesterol levels and decrease the cardio vascular risks.

Introduction

ANTIULCER ACTIVITY OF *MILAGATHY CHOORNAM*

The *Siddha* system is a treasure-house of secret science, gifted to the world by *siddhars. The siddhars* were pioneers in the world in the field of minerals, metals and medicinal herbs.

Siddhars have selected the drugs to treat the diseases by knowing the taste of the drugs and amalgamation of elements and knowing the vital *thathus.* In such an approach that is not only subsides the pathological signs and symptoms but also rectifies the root cause.

According to *siddhars* science, the three humours in their normal order occupy respectively the lower, middle and upper parts of the body and maintain their integrity-the vayu in the region of the pelvis and the rectum, the pitham in the region of the stomach and the internal viscera and the phlegam in the region of the breath, throat and head. The three humours maintain the upkeep of the human body through their coalesced function .When deranged they bring about diseases peculiar to their influence. When in equilibrium, freedom from diseases and when one or other of the humours combine in such a manner as to get deranged by aggravation diminution etc, disease or death may be the result.

Vatha, pitha and *kapha* have multiple significance and symbolical in terms

1. *Vatha* represents mind, dryness ,pain ,flatulence, lightness and also air.
2. *Pitha* represents gastric juice, bile, energy, heat, inflammation, anger and irritation ,etc.
3. *Kapha* represents feeling of cold, heaviness ,running of nose, passing of mucoid discharge and also the saliva

In modern world gastro intestinal disorders are the universal problem. *Oimmam* as explained by great s*iddhars* has clinical symptoms, closely related to peptic ulcer. The *Gunmam* is classified into eight varieties according to *Yugimuni Vaidya Chinthamani.*

The *'Gunmam'* means reduced state of metabolic and mental activities.

According to *siddha* the cause of most ulcers lies in a mixture of *vatha and pitha* provoking factor

It has been told by Therar as

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The factors, which assumed to affect this equilibrium are environment, climatic conditions, diet, physical activities, and stress.

So proper diet, medicine and a disciplined regimen of life are advised by *siddhars* for a healthy living and to restore equilibrium of humors in diseased condition

The term ' peptic ulcer ' refers to an ulcer in the lower oesophgus,stomah or duodenum,in the jejunum after surgical anastamosis to the stomach or, rarely,in the ileum adjacent to a Meckels diverticulum.-Davidson 's principles and practice of medicine-ll[81] edition. 2010.

Peptic ulcer occurs in that part of gastrointestinal tract which is exposed to gastric acid and pepsin,i.e.the stomach and duodenum.lt results probably due to an imbalance between the aggressive(acid,pepsin and bile) and the defensive(gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide,innate resistance of the mucosal cells) factors Medical pharmacology, KD Tripathy 6th edition. 2010

Hypersecretion of gastric acid is a pathological condition,which occurs due to uncontrolled secretion of hydrochloric acid from the parietal cells ofthe gastric mucosa through the proton pumping H+K+ATPase. Even the normal rate of acid secretion may cause ulceration in the breached mucosa when some gastro protective factors are lost.

Dieteric indiscretion such as overeating, taking of heavy meals or highly spiced foods, coffee, alcohol and smoking are the main factors contributing to this condition. Other causes are the ingestion of certain drugs, food poisoning, certain infections, gout, emotional disturbances, stress, and nervous tension

The modern approach to control gastric ulceration is to inhibit gastric acid secretion, to promote gastroprotection, block apoptosis and stimulate epithelial cell proliferation for effective healing. Most ofthe antisecretory drugs such as proton pumpinhibitors (omeprozole lansoprazole, etc.) and histamine H2-receptor blocker (ranitidine,famotidine, etc.) are extensively used to control increased acid secretion and acid related disorders . But there are reports of adverse effects and relapse in the long run.

On the contrary most of the siddha drugs reduces the offensive factors and are proved to be safe clinically effective, having better patient tolerance,relatively less expensive and globally competitive.

In *siddha* the treatment should be commenced as early as possible after evaluating the course and cause ofthe disease. Treatment is classified into three categories: *devamaruthuvum* (Divine method); manuda *maruthuvwn* (rational method); and *asura mamihuvum* (surgical method). In Divine method, medicines like parpam,chendoomm, guru,kuligai made of mercury, sulfur and pashanams are used. In the rational method, medicines made of herbs like choornam,kudineer or vadagam are used. In surgical method, incision, excision, heat application, blood letting, or leech application are used.

Choornas are fine dry powder of drugs. They are often easier to make for compounds that consist of many ingredients. Powders usually have quick action. They work mainly on the gastro intestinal tract and *rasa thatu* or plasma.Milagathi chooraam ,a herbo mineral formula which consist of *chukku(Zingiber* officinale, *milagu(Piper* nigrum), *thippili(Piper* longum), *karunjeeragam(Nigella. sativa), omam(Cummum cyminum), perungayam(Ferula. asafoetida*), Kadukkai(*Terminalia chebula*) *and indhuppu(Sodium* chloridelmpura). In that formula *indhuppu* is a mineral.

In siddha system,minerals are divided into three major divisions. They are *pashanam, Karasaram* and *uparasam. Karasaram (uppu)* are totally 25, out of this 15 are synthetic and 10 are natural salts.Indhuppu is one among the synthetic *karasaram. Karasarams* are of great medicinal value. Other herbals in this madicine are well known for their action on gastro intestinal tract. Every ingredient in this medicine *(milagathi choornam) has* the power to cure *gunmom* which has been clearly mentioned with their general characterestics as a script in *Agathiar guna vagadam* .So the author has decided to see the efficacy of the milagathi choornam in the clinical study of antiulcer activity

Aim & Objectives

CHAPTER I

AIM & OBJECTIVE

1. Aim :

To validate the safety and efficacy of *Milagathi Choornam* in the management of Peptic ulcer

2. Objectives:

In this dissertation work, the ***"MILAGATHI CHOORANAM'*** is analyzed in

the following aspects:

- Standardization of *Milagathi choornam* including pharmacognostic characterization of raw drug and purity analyses
- Safety profile for the test drug in rodents
- Pharmacological study to evaluate the anti-ulcer activity in rat
- Open clinical study to assess the safety and efficacy of the drug on Peptic ulcer patients.

Review of Literature

CHAPTER II

REVIEW OF LITERATURE

Indhuppu

Sodium chloride impura

Vernacular names

English - Rock Salt;Sea salt:Bay salt;Sodium chlorate

Tamil - *Indu-uppu*

Hindi - *Sedhalon;Sendhalon*

Sans - Saindhava

Arab - Mil-he-tabazard

Ger - Natrium chloricum

Tel - Saindhalavanam

Mal - Intu-uppu

Source

Found in nature in extensive bed mostly associated with clay and calcium sulphate. To obtain a, holes are dug into these rocks which soon become filled up with salt water; the water is evaporated and the salt is left ready for use.

Character

It is found in small white crystalline grains or transparent cubes. It is brownish white externally and white internally. It has pure saline taste and burns with a yellow flame.

Action

In small dozes it is highly **carminative**, stomachic and **digestiv**e.It promotes the appetite and assists digestion and assimilation. In large doses(1-2drachms)it is cathartic;in still larger doses(4-8drachms)it is emetic.

Uses

It is given in dyspepsia and abdominal disorders.

A compound powder called Vadavanal churna containing rock salt, long pepper, pipli, cubeb, chitrak,ginger and myrobalans in equal parts, mixed and made into a powder used in anorexia, flatulence and biliousness.

Dose-5 to 15 grains two or three times a day with water.

PREPARATIONS

Thengaisharam

Take a coconut fruit full of water make hole in it and fill the coconut with rock salt and dissolve it in it water. Then close the opening, cover the nut with a layer of clay and roast in a pit of fire. The salt thus roasted is given with the addition of long pepper.

Dose: Quarter tola

Uses: It is valuable in the form of dyspepsia which is attended with pain two or three hours after meals.

A powder made of rock salt 10 grains kaladana scale 1 drachm and dry ginger 10 grains is a good laxative in a single dose.

As a digestive a compound powder made of rock salt, chebulic myrobalan, emblic myrobaln and long pepper in equal part is recommended in dose 10 grains twice a day.

A powder containing pancha lavana 5 parts impure oxide of iron 5 parts and emblic myrobaln 4 parts is useful in doses of 10 grains in dyspepsia, congested liver etc.

(Ref:Dr.K.M.Nadkarni&s Indian material medica Volume-2 page no:108)

General character-indhuppu

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Induppu is specially given for eight types of ulcer. kabha diseases, constipation, eczema are cured by Indhuppu

Preparations that contain Indhuppu

Indhuppu choornam

Indhuppu	-	1part
Cuminum cyminum	-	1part
Trachyspermum ammi	-	4parts
Piper longum	-	4parts
Zingiber officinale	-	16parts
Terminalia chebula	-	32parts

All the above powders are mixed well

Dose : 12gms

Uses : Indigestion,vomiting,ascites.

2) PANCHALAVANA CHUNNAM

Savukkaram	-	1part
Valayulluppu	-	1/4part
Indhuppu	-	1/4part

Vengaram - 1/4part

Kariuppu - 1/4part

All the above are rubbed rogether in a kalvam with amuri made into villai.then enclosed in agal and subjected to putam with 5varratties

Dose : 650mg

Uses : abdominal pain, ulcer

CHUKKU

Botanical name: Zingiber officinale

Family : Zingiberaceae

VERNACULAR NAMES

English : Dried ginger

Hind : Sonth

Tel : Sonti

Mal : chukku

Dried Ginger is Called *Chukku*

Part used : Rhizome

Actions : Stimulant, Stomachic, Carminative

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Dried ginger powder is mixed with sugarcane juice.when it is given in the morning. It relieves **burning stomach.**Dicoction of the dried ginger is always good for health.

Chemical constituents

Aromatic volatile oil, The volatile oil contains camphene and phallandrene, Zingiberine, Cineol, Berneol, Gingerin, Gingerol, Resin, Starch

Uses

Dried ginger is aromatic, and carminative, produces a sensation of warmth at the epigastrium and expels flatus. As a carminative it is given in colic The dry rhizome powdered and made into a paste with warm water is used as a cataplasm or fomentation to the forehead in headaches, neuralgia, colic and toothache; also given in dyspepsia, loss of appetite, to correct the flatulence in colic,diarrhea etc.

Research highlights

Anti ulcer principle in ginger. An anti ulcer compound 6 gingesulphonic acid and three mono acyldigalactosyglycerols, Gingeglycolipids A,B, and C are isolated from dried rhizome of zingiber officinale which was cultivated in Taiwan .

The phenolic constituents of the alcohol soluble fraction in responsible for its anti oxidant effect. (YoshikanM et.al,)

MILAGU

Botanical name: *Piper nigrum*

Family :Piperaeae

VERNACULAR NAMES

Eng : Black pepper

Hind: Kall-mirch

Mal : Kurumulaku

Pers: Flifliaisiah

Kan: Menasu

Part used: Seeds

Actions:

Acrid, Carminative, Antiperiodic, Rubefacient, Stimulant, Resolvent, Antivatha, Antidote

General character of *Piper nigrum*

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Pepper cures fever, anemia, kabam, dysentry, ulcer, vatham

Uses

Black pepper as culinary spice and condiment is well known throughout the world. Black pepper growing in Malabar cost is the best, and as stimulant and carminative is prescribed in choleras, dyspepsia, flatulence, diarrohea and various gastric ailments.

Black pepper is useful for dyspepsia and flatulence when taken ten to fifteen grains.

(Ref:Dr.K.M.Nadkarni & Indian material medica)

CHEMICAL CONSTITUENTS

Black pepper contains volatile oil and piperine, piperidine, piperettine, and a few other minor alkaloids (piperyline, piperolein A, piperolein B, piperanine, etc.).Piperine and piperanine are the known pungent principles.

Chavicine and many other amide alkaloids have recently been isolated, for example, pipwaqarine, piptigrine, pipnoohine, pipyahyine, pellitorine, guineensine, pipercide, retrofractamide A, dipiperamides D and E and others.

Black pepper is also reported to contain flavonol glycosides (especially those of kaempferol, rhamnetin, and quercetin) in considerable concentration, as well as sterols (stigmastane-3, 6-dione and stigmast-4-ene-3,6-dione) and polysaccharides. Pepper oil contains a complex mixture of monoterpenes (70–80%), sesquiterpenes (20–30%), and small amounts of oxygenated compounds, with no pungent principles present. Concentration and composition vary, depending on sources. Major monoterpenes include α-thujene, α-pinene, camphene, sabinene, β-pinene, myrcene, 3-carene, limonene, and β-phellandrene. Sesquiterpenes include β-caryophyllene (major component), β-bisabolene, β-farnesene, *ar*-curcumene, humulene, β-selinene, α-selinene, β-elemene; α-cubebene, α-copaene, and sesquisabinene. Oxygenated components include linalool, l-terpinen-4-ol, myristicin, nerolidol, safrole, β-pinone, and *N*-formypiperidine, among others.

Thippili

Botanical name : Piper longum

Family : Piperaceae

Vernacular Names

Eng : Long pepper

Tel : *Pippillu*

Mal : *Thippili*

Kan : *Hippili*

Part used : Fruit

Action : Stimulant , Carminative

General character of *Piper longum*

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Preparation and uses

A common use of Piper longum in Indian medicine is for the prevention of recurrent attack of bronchhial asthma recurrent infection of throat and for flatulence and dyspepsia

(Ref**:** Indian herbal remedies) Active principles and pharmacology

Fruit gave alkaloids

N – isobutyldeca – trans 2, trans 4 diananmide

Essential oil from fruit contain n-hexadecane,n-heptadecane,n-nonadecane

p-cymene,L-tyrosene,L-cysteine hydrochloride

(Ref**:** Indian herbal remedies C.P.Khare)

Omum

Botanical name : Trachyspermum ammi

Family : Apiaceae

Vernacular Names

Eng : Bishop’s weed

Hin : Ajowan, Ajwan

Tel : Vaamu

Tam : Omum, Asampadam , Amam

Mal : Omum, Ayamodakam

Part used : Seed

Actions : Anthelmintic, Antiseptic, Stomachic, Antispasmodic**,** Carminative, Sialogouge, Stimulant, Antiseptic, Tonic

CHEMICAL CONSTITUENT

1. Ajowan fruits contain 2-4% of volatile oil about 21% of fat,17% proteins and 25% carbohydrate, trace of tannin, glycoside and steroidal substances have been reported

2. Volatile oil mainly contains Thymol (35-60%), P-Cymene 50-55%, Terpinene 30-35%, Pinene, Dipenetenes etc, are other constituents of the oil. The flavor and taste of drug is due to thymol and volatile oil

PROPERTIES AND USES

1. It is administered in flatulence, atonic,dyspepsia ,diarrhea and often recommended for cholera
2. It has been shown to possess antibiotic activity against salmonella typhi Micrococcus pyogenes variant aureus and Escherichia coli
3. Ajowan is used as a house hold remedy for indigestion
4. Oma water which is commonly used in India as a carminative and is useful in flatulence and griping, especially in children. The water left over after the essential oil and thymol have been removed from the steam distillate

Reference - Indigenous Drugs of India – Chopra R.N

Karunjchirakam:

Botonical name : Nigella sativa linn

Family : Ranunculaceae

Vernacular Names

Eng : Black cumin

Hind : *Kulanji*

Tel : *Nalla – jilakarra*

Mal : *Karinchirakam*

Kan : *Karl-jirige*

Part Used: Seeds

Action : Carminative, Diuretic, Emmenagogue, Galactogogue, Anthelmintic, Stomachic, Parasiticide, Emollient

Chemical Constituents

Black cumin seeds contain a bitter principle nigellin, tannins, reducing sugar mostly gluose saponins and Arabic acids and other alcohol-soluble organic acid. The free amino acid present in dormant seed are cystine, lysine, aspartic acid, glutamic acid, alanine, tryptophan, valine and leucine;

(Indian herbal remedies K.P.Khare)

Kadukkai

Botanical name: *Terminalia chebula*

Vernacular names

English : Chebulic Myrobalan

Tamil : Kadukkai

Sanskrit : Haritaki, Priya, Sudha

Hindhi : Pile Hara

Pers : Haleelai Siah

Kan : Anile-Kayl

Tel : Chitti karakkaya

Mal : Katuukkaipinja

Kadukkukkai embodies all the taste except salt. According siddha it is classified into seven types. They are

Vijaya : looks just a squash and can be used in any case.
Rohini : is round in shape and more effective for healing.
Putana : is small in size with big hard seeds, and is useful for external plastering.
Amrita : is fleshier, and good for body purification.
Abhaya : has five lobes, and is more effective for ophthalmic use (external).
Jivanti : is yellow in color and good for all cases.
Chetaki : has three lobes, is good to use in the form of powder, and is more laxative than the others. Chetaki comes in two varieties

Preparation and Uses

Kadukkai vadagam:

Dose : 1or 2

Uses : vomiting, **peptic ulcer**, asthma,piles

Pavana kadukkai

Uses : cough, peptic ulcer, asthma, vomiting, piles

Active Principles and Pharmacology

Fruit contain chebulinic acid,tannic acid and chebulin Oil from kernels yielded palmitic, searic,oleic, linoleic, arachidic and behenic acids. Antioxidant constituents of the plant, phloroglucinol and pyrogallol, have been isolated along with ferulic, vanillic, p-coumaric and caffeic acids.

Ether extract showed higher antioxidant activity than BHA and BHT.Acid esters present in phenolic fraction of extract were found more effective.

A new ellagitannin-terchebulin-has been isolated from fruits along with punicalagin and terflavin A and its structure has been elucidated.Terflavins B,C and D,punicalagin and punicalin have been isolated from leaves.

Gallic,triacontanoic and palmitic acids,beta-sitosterol, doucosterol,riehyl ester of gallic acid from fuits have been isolated.A new triterpene-chebupentol-has been isolated from fruits;arjungenin,terminoic acid arjunolic acid have been isolated.

The oil in the kernel increased the motility of the gastrointestinal tract of the mouse. The action was comparable with castor oil.The oil itself is non irritant,but releases an irritant principle when incubated with lipase

(Indian herbal remedies) c.p.khare 2004

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Disease review-Modern aspect

Peptic ulcer disease

The term ´Peptic ulcer ´ refers to an ulcer in the lower oesophagus, stomach or duodenum in the jejunum after surgical anastomosis to the stomach or , rarely , in the ileum adjacent to Meckel's diverticulum.

It results probably due to an imbalance between the aggressive (acid, pepsin,bile and H.pylori) and the defensive(gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide , innate resistance of the mucosal cells) factors.

Etiology of peptic ulcer:

Hereditary:

Genetic & blood group: run in families espcially blood group (3: 1) of other blood groups, ABO gene may modify the size of parietal cell mass

Dietary habits:

Spicy foods, Vitamin A deficiency

Non Steriodal Anti Inflammatory Drugs:

Accounts to 3 % of ulcers

Smoking and alcohol:

Due to inhibition of pancreatic bicarbonate by nicotine with increased risk of complication.

Helicobacterium Pylori:

Submucous spirochetal bacteria split urea to ammonia. The high alkalinity of ammonia stimulate G cells to secrete gastrin which reduces the resistance of gastric mucosa

Psycosomatic factors:

Stress and anxiety due to Burns, CNS trauma, Surgery and severe medical illness

Hormonal factors:

Hyperparathyroidism increase in Ca increase HCl,Hormonal over secretion by islets of pancreas to secrete gastrin in excess. (Zollinger-Ellison Syndrome).

Pathology:

Incidence	:	male more than female.
Duodenal	:	Gastric 4: 1
Site	:	Lesser curvature of stomach, First part of the duodenum
Size	:	Less than 1 inch
Shape	:	Usually oval or rounded.

Clinical Features:

Recurrent abdominal pain which has 3 notable characteristic

1) Pain in epigastrium
2) Pain starts within three hours of eating food and it may be described as burning, aching pressure, fullness or as a sensation of hunger
3) Pain may be more prominent at night, the pain is usually relieved by food, antacids, or even by vomiting.

Physical examination

Tenderness in the epigastrium or to the right of the midline. Ulcer patients are able to localize the pain and this feature helps to distinguish them from cases of functional dyspepsia.

Differential diagnosis

Epigastric pain is the common symptom in several alimentary disorders such as

1. Gastric carcinoma
2. Pancreatic carcinoma
3. Pancreatitis
4. Biliary tract disease
5. Peptic ulceration of the esophagus
6. Tiuodentitis
7. Ancylostomiasis

Complications

1. Hematemesis
2. Melena
3. Pyloric obstruction
4. Perforation
5. Pancreatitis

Investigations of peptic ulcer:

- CBC
- Double contrast barium meal examination
- Upper GI endoscopy
- H. Pylori

Serologic antibody test for HP,

- Fecal antigen test tests for active HP
- Urea breath test tests for active HP

Life style modifications:

1. To avoid smoking, alcohol, betal nut chewing ,Coffee, Tobacco
2. Timely intake of food, avoiding oily and fried foods
3. Smoking and alcohol cessation
4. Stress reduction
5. Discontinue NSAIDs

Materials & Methods

CHAPTER III

MATERIALS AND METHODS

1. STANDARDIZATION OF MILAGATHI CHOORNAM

1.1 Materials:

Milagathichooranam has been selected from the classical *siddha* literature " ***Maruthuva asiriyam"(*****page.no.66),Publisher.**T.Mohan Raj.Ingredients of the test drug are as follows:

1. *Sodium chloride impura*
2. *Zingiber officinale*
3. *Piper nigrum*
4. *Piper longum*
5. *Trachyspermum ammi*
6. *Ferula asafetida*
7. *Nigella sativa*
8. *Terminalia chebula*

1.2 Collection of the drugs:

Trachyspermum ammi:

250 gram of the raw drug was collected from the Tampcol raw drug store at Chennai. The adulteration particles were cleaned well.

Sodium chloride impura:

250 gram of the raw drug was collected from the Tampcol raw drug store at Chennai. The adulteration particles were cleaned well.

Piper longum:

250 gram of the raw drug was collected from the Tampcol raw drug store at Chennai. The adulteration particles were cleaned well.

Terminalia chebula:

500 gram of the raw drug were collected from the Tampcol raw drug store at Chennai. The adulteration particles were cleaned well.

Ferula asafetida

*:*500 gram of the raw drug were collected from the Tampcol raw drug store at Chennai. The adulteration particles were cleaned well.

Nigella sativa:

500 gram of the raw drug was collected from the Tampcol raw drug *store at Chennai.*

Zingiber officinale

500 gram of the raw drug was collected from the Tampcol raw drug store at Chennai.

Piper longum

500 gram of the raw drug was collected from the Tampcol raw drug store at Chennai.

All materials were identified and confirmed by the Head of the Gunapadam department, GSMC, Chennai.

1.3 Purification of the raw materials:

1. Sodium chloride impura**:** Soaked in vinegar for 3 days and then dried under the sun.
2. *Piper longum* **:** soaked in lemon juice and then dried under the sun
3. *Zingiber officinale:* skin is peeled off
4. *Piper longum:* Soaked in vinegar and then dried under the sun.
5. *Trachyspermum ammi* : soaked in lime stone water for 3 hours and then fried

6. *Ferula asafoetida :* Asafoetida is fried

7. *Terminalia chebula:*

Seeds were removed, and rinds part only used.

8. *Nigella sativa:* Fried

1.4 Preparation of *Milagathi chooranam:*

After purification process, each material should be complete dried and was powdered separately by grinding method. Those powder was sieved by white cloth (*Vasthirakayam).*

Preservation:

The purified *Chooranam* was stored in a clean, air tight glass container.

Life span :

3 Months.

Administration of the drug:

Form of the medicine : Chooranam

Route of Administration : Enteral

Dose : 500 mg

Anubanam (Vehicle) : With food

Time of Administration : Two times a day with food

INGREDIENTS OF *MILAGATHI CHOORNAM*

Fig1 Karunjeeragam

Fig2 Kadukkai

Fig3 Thippili

Fig4 Chukku

Fig5 Induppu

Fig6 Omam

Fig7 Perungayam

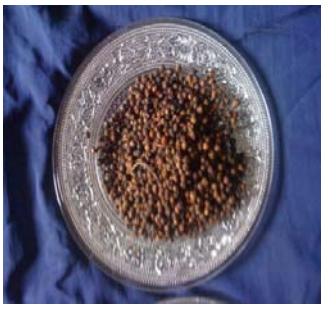


Fig8 Milagu

1.5 Physico chemical analyses

1.5(a) Physico chemical parameters

Determination of Total Ash

3 g of the powder was incinerated in a silica dish at a temperature not exceeding 450º until free from carbon, cool and weigh. The percentage of ash was calculated with reference to the air-dried drug.

Determination of Acid Insoluble Ash

The obtained ash was boiled for 5 minutes with 25 ml of dilute hydrochloric acid and insoluble matter was collected in ashless filter paper. Then, it was washed with hot water and ignited to constant weight. The percentage of acid-insoluble ash was calculated with reference to the air dried drug.

Determination of Alcohol Soluble Extractive

5 g of powder was mixed with 100 ml of Ethanol of the specified strength in a closed flask and kept alone for twenty-four hours. Filtered rapidly with taking precautions against loss of solvent. 25 ml of the filtrate was evaporated to dryness in a tared flat bottomed shallow dish, and dried at 105º, to constant weight and weighed. The percentage of alcohol-soluble extractive was calculated with reference to the air-dried drug.

Determination of Water Soluble Extractive

5 g of powder was mixed with 100 ml of chloroform water of the specified strength in a closed flask and kept alone for twenty-four hours. Filtered rapidly with taking precautions against loss of solvent. 25 ml of the filtrate was evaporated to dryness in a tared flat bottomed shallow dish, and dried at 105º, to constant weight and weighed. The percentage of water-soluble extractive was calculated with reference to the air-dried drug.

Determination of Moisture Content (Loss on Drying)

10 g of drug was taken in the tared evaporating dish and dried at 105º for 5 hours, and weighed. (Continue the drying and weighing at one hour interval until difference between two successive weighing corresponds to not more than 0.25 per cent. Constant weight is reached when two consecutive weighing after drying for 30 minutes and cooling for 30 minutes in a desiccator, show not more than 0.01 g difference).

***Potential of Hydrogen* (pH)**

The pH scale is logarithmic and runs from 0.0 to 14.0 with 7.0 being neutral. Readings less than 7.0 indicate acidic solutions, while higher readings indicate alkaline or base solutions.

1.4(b) THIN LAYER CHROMATOGRAPHY

Solvent system

Toluene : Ethyl acetate: Acetic acid (5 : 5 : 0.5).

TLC plate

Aluminium plate precoated with silica gel $60F_{254}$ of 0.2 mm thickness (Merck).

Developing chamber

Camag's twin trough chamber.

Visualizing reagent

Vanillin-sulphuric acid reagent.

Extract Preparation

4 g of the chooranam was soaked overnight in chloroform. Boiled on a water bath for 10 mins, filtered and concentrated to 10 ml.

Procedure

The extract was applied on the TLC using capillary and developed in the solvent system. The developed TLC plate was air dried and photograph was taken in white light. Then dipped in vanillin-sulphuric acid reagent, heated in an oven at 105°C until the development of coloured spots and photograph taken.

1.4 (c). Qualitative Phytochemical Analysis:

S.No	EXPERIMENT	OBSERVATION	INFERENCE
1.	**Test for Alkaloids:** Alkaloids are identified by precipitate method **Dragendroff's reagent:** An aqueous plant extract of 2 ml is mixed with 2 ml of Dragendroff's reagent.	Prsence of reddish brown precipitate	Presence of alkaloids
2.	**Test for Triterpenoids (Noller's Test)** To few mg of extract, add tin and thionyl chloride and heat in water bath.	Absence of purple colour	Absence of Triterpenes
3.	**Test for Tannins:**A plant sample dried powder 0.5 gm is boiled in 20 ml of water and filtered. The filterate 2 ml is taken and 3-5 drops of $Fecl_2$ (0.1%) is slowly added to it.	Forms a brownish-green or bluish- black colour.	Presence of Tannins
4.	**Test for Flavonoids:** An aqueous filterate of plant	Presence of Yellow	Presence of

	sample is mixed with 5 ml of dilute Ammonium solution and few drops of concentrated H_2SO_4 is slowly added through the sides of the test tube.	colour formed	flavonoids
6.	**Test for Glycosides:**An aqueous plant extract of 2 ml is added with 1 ml of concentrated Hcl and boiled in a water bath for about 2 hours. The filtrate is separated and 3 ml of chloroform is added, then 10% of 1ml Ammonium solution is added.	Absence of pink colour formation	Absence of glycosides
7.	**Test for Saponin:** A powdered 2 gm of plant sample is boiled with 20 ml of distilled water, then filtered, the filterate is added with fresh 5 ml of distilled water and shaken vigorously.	A permenant or persistant froth is formed.The froth is turned in to emulsion by adding three drops of olive oil.	Presence of saponin
8.	**Test for Phenolic compounds:** About 2 ml of aqueous plant extract is mixed with 2 ml of $Fecl_3$ solution.	Presence of deep bluish green colour	Presence of phenolic compounds

Methodology for Chemical Analysis

Preparation of Extract :

Add 5 gm of the sample to 50ml of distilled water. Boil the solution for 20 minutes, cool and then filter. Use the Extract for the following tests.

S.No	Experiment	Observation	Inference
1.	**Test for reducing Sugar :** To 5ml of Benedicts qualitative reagent, add 10 drops of extract, then boil for two minutes	Green / Yellow / Red PPT	Presence of Reducing Sugar
2.	**Test for Starch :** To 5 ml of extract add 2ml of acetic acid and then add few drops of N/50 Iodine Solution.	Blue Colour	Presence of Starch
3.	**Test for Proteins :** To 2 ml of extract, add 2ml of 5% Sodium Hydroxide mix and add 2 drops of Copper Sulphate Solution.	Violet or Purple Colour	Presence of Proteins
4.	**Test for Amino Acid :** Place 2 drops of extract on a filter paper and allow to dry well. Then spray 1% ninhydrin over the same and allow to dry.	Violet Colour	Presence of Amino Acid
5.	**Test for Albumin :** To 2 ml of extract, add 2ml of Esboch's reagent.	Yellow PPT	Presence of Albumin

6.	**Test for Phosphate :** To 2ml of extract, add 2ml of ammonium Molybdate solution and 2ml of concentrated Nitric Acid.	Yellow PPT	Presence of Phosphate
7.	**Test for Sulphate :** To 2 ml of extract add 2ml of 4% ammonium oxalate solution.	White PPT	Presence of Sulphate
8.	**Test for Chloride :** Add 2ml of extract to dilute nitric acid till the effervescence ceases. Then add 2 ml of Silver Nitrate Solution.	Cloudy White PPT	Presence of Chloride
9.	**Test for Iron :** To 2ml of extract, add 2ml of ammonium thio cynate solution and add 2ml of concentrated Nitric Acid.	Red Colour	Presence of Iron
10.	**Test for Calcium :** To 2 ml of extract, add 2 ml of 4% ammonium Oxalate Solution.	White PPT	Presence of Calcium
11.	**Test for Sodium :** Make a paste with 2 pinches of the sample with Hcl and Introduce it into the blue flame.	Yellow Flame	Presence of Sodium

12.	**Test for Potassium :** Add a pinch of the sample to 2 ml of Sodium Nitrate Solution. Then add 2ml of Cobal Nitrate in 20% acetic acid.	Yellow PPT	Presence of Potassium
13.	**Test for Zinc :** To 2ml of extract, add few drops of Sodium Hydroxide.	White PPT	Presence of Zinc
14.	**Test for Magnesium :** To 2ml of extract, add few drops of Sodium Hydroxide Solution	White PPT	Presence of Magnesium
15.	**Test for Alkaloids :** a. To 2ml of extract, add 2ml of Potassium Iodide Solution b. To 2ml of extract add 2ml of Picric Acid. c. To 2 ml of extract add 2ml of Phosphotunqstic Acid.	Red Colour Yellow Colour White PPT	Presence of Alkaloids Presence of Alkaloids Presence of Alkaloids
16.	**Test for Tannic Acid :** To 2ml of extract add 2 ml of Ferric Chloride Solution	Black PPT	Presence of Tannic Acid

1.4 (d) FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR):

INSTRUMENT DETAILS:

Model	**:**	**Spectrum one: FT-IR Spectrometer**
Scan Range	**:**	**MIR 450-4000 cm-1**
Resolution	**:**	**1.0 cm-1**
Sample required	**:**	**50 mg, solid or liquid.**

Fourier Transform Infrared Spectroscopy (FTIR) is an analytical technique used to identify mainly organic materials. FTIR analysis results in absorption spectra which provide information about the chemical bonds and molecular structure of a material. The FTIR spectrum is equivalent to the "fingerprint" of the material and can be compared with cataloged FTIR spectra to identify the material.

Infrared spectrum is useful in identifying the functional groups like -OH, -CN, -CO, -CH, -NH2, etc. Also quantitative estimation is possible in certain cases for chemicals, pharmaceuticals, petroleum products, etc. Resins from industries, water and rubber samples can be analyzed.

1.4(e) SCANNING ELECTRON MICROSCOPE (SEM):

The Scanning Electron Microscope (SEM) is a microscope that was electrons rather than light to form an image. There are many advantages to using the SEM instead of a light microscope.

Resolution : 1.2 nm gold particle separation on a carbon substrate

Magnification : From a min of 12 x to greater than 1, 00,000 X

The SEM has a large depth of field, which allows a large amount of the sample to be in focus at one time. The SEM also produces images of high resolution, which means that closely spaced features can be examined at a high magnification. Preparation of the samples is relatively easy since most SEM one require the sample to be conductive.

The combination of higher magnification, larger depth of focus, greater resolution, and easy of sample observation marks the SEM one of the most heavily used instruments in research areas today.

2. TOXICOLOGICAL AND PHARMACOLOGICAL STUDIES

Animals

Albino mice of either sex weighing 25-30g (For acute toxicity study) and Healthy Swiss Albino rats of the Wister strain weighing 150-200 g were used for the study. The animals were used with the approval of the Institute animal ethics committee and obtained from Vels University, Chennai. They were fed with a balanced standard pellet diet and maintained under standard laboratory conditions, providing 24-28^{0}C temperature, standard light cycle (12 h light, 12 h dark) and water ad libitum.

Animals were kept in cages with raised floors of wide mesh to prevent coprophagy. Animal welfare guidelines were observed during the maintenance period and experimentation. The rats were randomly assigned to control and different treatment groups, six animals per group. The experimental protocol used in this study was approved by IAEC. (XIII/VELS/PCOL/08/2000/CPCSEA/IAEC/08.08.2012). The animals were acclimatized for one week under laboratory conditions.

Acute toxicity study:

Acute oral toxicity test for the Milakathi Chooranam was carried out as per OECD Guidelines 425. As with other sequential test designs, care was taken to ensure that animals are available in the appropriate size and age range for the entire study. The test substance is administered in a single dose by gavage using a stomach tube or a suitable intubation cannula. The fasted body weight of each animal is determined and the dose is calculated according to the body weight. After the substance has been administered, food was withheld for a further 2 hours in mice. Single animals are dosed in sequence usually at 48 h intervals.

However, the time interval between dosing is determined by the onset, duration, and severity of toxic signs. Treatment of an animal at the next dose was delayed until one is confident of survival of the previously dosed animal. The time interval was adjusted as appropriately in case of inconclusive response. The test is simpler to implement when a single time interval is used for making sequential dosing decisions. Special attention was given during the first 4 hours and daily thereafter, for

a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead.

All observations are systematically recorded and Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behaviour pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. Animals found in a moribund condition and animals showing severe pain or enduring signs of severe distress was humanely killed. When animals are killed for humane reasons or found dead, the time of death was recorded

SUB-ACUTE TOXICITY

In a 28-days sub acute toxicity study, twenty four either sex (3+3) rats were divided into four groups of 6 rats each. Group I that served as normal control was administered with distilled water (p.o.) while groups II, III and IV were administered daily with the Milakathi Chooranam (p.o.) for 28 days at a dose of 0.1, 0.2 and 0.4g/kg respectively. The animals were then observed daily for gross behavioural changes and any other signs of subacute toxicity. The weight of each rat was recorded on day 0 and weekly throughout the course of the study, food and water consumption per rat was calculated. At the end of the 28 days they were fasted overnight, each animal was anaesthetized with diethylether, following which they were then dissected and blood samples were obtained by cardiac puncture into heparinised tubes. The blood sample collected from each rat was centrifuged with 3000 X g at 4^{o}C for 10 min to separate the serum and used for the biochemical assays.

Hematological and blood biochemical analyses:

At the end of the study, all animals were kept fasted for 16-18 h and then anesthetized with anesthetic ether on the 28th day. Blood samples for hematological and blood chemical analyses were taken from retro orbital vein. Heparinized blood samples were taken for determining complete blood count (white blood cell count, differential white blood cell count, platelet count, red blood cell count, hematocrit, and hemoglobin) by semiautomated hematology analyzer. The serum from non-heparinized blood was carefully collected for blood chemistry and enzyme analysis

(glucose, creatinine, total protein, albumin, total and direct bilirubins, serum glutamate-oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and alkaline phosphatase (ALP)) were automatically determined using autoanalyzer.

Necropsy:

All rats were sacrificed after the blood collection. The positions, shapes, sizes and colors of internal organs were evaluated. The Spleen, Testes, Pancrea, Lung, Liver, Brain, Heart, Stomach, Intestine, Bone, Ovary, and Kidney tissues were excised from all rats to visually detect gross lesions, and weighed to determine relative organs' weights and preserved in 10% neutral formalin for histopathological assessment. The tissues were embedded in paraffin, and then sectioned, stained with haematoxylin and eosin and were examined microscopically.

Statistical analysis

Values were represented as mean ± SEM. Data were analysed using one-way analysis of variance (ANOVA) and group means were compared using the Tukey-Kramer Multiple Comparisms Test using GraphPad Instat-V3 software. P values < 0.05 were considered significant.

2.3 Screening the efficacy of Milagathy Choornam on Aspirin induced Peptic ulcer rodents

Procedure

Aspirin induced Peptic ulcer:

Animals were divided into 5 groups (n = 6). Group I (Normal) treated with distilled water 5 ml/po. Group II (Control) treated with Carboxy methyl cellulose mixed with distilled water 5 ml/po. Group III (Test drug) treated with Milagathi Chooranam 250 mg/kg mixed with distilled water 5 ml/po and Group IV (Test drug) treated with Milagathi Chooranam 500 mg/kg mixed with distilled water 5 ml/po. Group V (Standard) treated with Ranitidine 60 mg/kg mixed with distilled water 5 ml/po. All groups received treatment 30 min prior to the oral administration of aspirin (400mg/kg). The animals were scarified, after 6 hours following the administration of

aspirin, stomachs were removed and 2% formalin was injected into the stomach. The stomach was open along with greater curvature and immersed in 2% formalin solution.

The length of each lesion was measured under the dissecting microscope. The sum of the length (mm) of all lesions for each rat was used in lesion index. The ulcer score was determined by using a 10 × magnifying hand lens. The scoring of severity of ulceration was as follows: 1 mm (pin point) = 1; 1-2 mm = 2; > 2 mm = 3; > 3 mm = 4. The mean ulcer score was determined by dividing the total ulcer indices in a group by the total number of animals in that group. Ulcer Score = Total ulcer index (UI) in a group/Total number of animals in that group.

3. CLINICAL STUDY OF *MILAGATHI CHOORNAM*

3.1 Objectives

`The study was conducted on hyperlipidemic patients to assess the hypolipidemic activity of ***"MILAGATHY CHOORANAM"*** clinically, both in-patients and outpatients of both sex and varying age groups.

3.2 Study Centre

The clinical study for **PEPTIC ULCER** is carried out in outpatient department and in patient ward of Govt.Siddha medical college hospital and Arignar Anna Indian Hospital, Arumbakkam, Chennai-106.

3.3 Design of the study:

Open clinical trial, phase II B

3.4 Selection:

51 patients from both sexes of various age groups were selected for clinical trial. Among 50 patients, 40 patients were treated as out-patients, 11 patients were treated as in– patients. The selection was based on the including and excluding criteria. They were clinically diagnosed on the basis of siddha principles with modern laboratory findings.

3.5 Registration Process

To register a patient, the following document has been proceeded.

- Copy of required laboratory tests
- Signed patient consent form then I verified eligibility and assigned a patient study number, drug dose and registered the patient on the study.

3.6 Selection Criteria:

Inclusion Criteria:

- Epigastric pain
- Heart burn

- Regurgitation
- Nausea/vomiting
- Loss of appetite
- Abdominal discomfort

Exclusion Criteria:

- Complication of peptic ulcer such as
    1. Haemorrhage,
    2. Perforation,
    3. Gastric outlet obstruction
- Radiating abdominal pain as in pancreatitis, appendicitis
- Acute abdominal colic's
- Cancer of the stomach
- Gall stone and hiatus hernia
- Cirrhosis of liver and jaundice

3.7 Criteria for Withdrawal:

Patients were removed from study when any of the criteria listed below applies. The reason for study removal and the date the patient was removed must be documented in the Case Report Form.

- Irregular medication.
- Patients who are all not cooperating to take blood samples.
- Any adverse reactions during the study period.
- Patients who are all not following the diet restrictions
- Patient decides to withdraw from the study, or Unwanted prolonged illness during the study period

3.8 Investigations:

For all the cases full clinical data were recorded and they were diagnosed on the basis of *SIDDHA* principles i.e. *Envagai Thrvugal*, *Ezhu Udal Thathukkal* Etc.

All the patients under study were subjected to blood investigations for TC, DC, ESR, and Hb.

Blood urea, serum cholesterol and Blood sugar were also investigated.

Urine test for albumin, sugar, deposits and motion test for ova, cysts were done.

The disease *GUNMAM* was confirmed in the patients by means of Endoscope examination, Barium meal examination and clinically.

Administration of the drug:

Form of the medicine : Chooranam

Route of Administration : Enteral

Dose : 500 mg

Anubanam (Vehicle) : With food

Diet and Medical Advice:

Do's and Don'ts:

Do's:

- Timely food
- Banana
- Almond milk
- Raw goat's milk
- Carrots and cabbage juice
- Butter milk
- He should chew every morsel thoroughly
- Meals must be small and frequent

Dont's

- Intake of food stuff during stress and anxiety
- Foods and drinks which are too hot or cold can be avoided
- Spicy foods, carbonated drinks
- Smoking and consumption of alcohol
- Intake of steroids and NSAIDS.

  Follow up

3.12 Trial Conduct:

This study will be conducted in compliance with the protocol approved by the Institutional Review Board, and according to Good Clinical Practice standards. No deviation from the protocol will be implemented without the prior review and approval of the IEC except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported to the IEC as soon as possible.

3.13 Criteria for Assessment of Response to Therapy:

1) Marked Relief : 95% relief in signs and symptoms and marked normalcy of pathological investigations.
2) Moderate Relief : 80% – 90% relief in the presenting signs and symptoms and moderate normalcy of pathological investigation.
3) Mild Relief : 70% - 80% relief signs and symptoms, mild normalcy of pathological investigation.
4) Poor Relief : below 60% relief of signs and symptoms and no marked changes in pathological investigations.

3.14 **Ethical Review**

The protocol and amendments were submitted to the Govt siddha medical college, Institutional Ethical Committee (IEC) and got formal approval for conducting the study. The decision of the IEC concerning the conduct of the study was made in writing to the investigator.

All subjects for this study was provided a consent form describing this study and provided sufficient information for subjects to make an informed decision about their participation in this study. This consent form was submitted with the protocol for review and approval by the IEC. The formal consent of a subject, using the IEC-approved consent form, was obtained before that subject is submitted to any study procedure. This consent form was signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

Results & Discussion

CHAPTER IV

RESULTS AND DISCUSSION

The well documented *Siddha* herbo – mineral drug *Milagathi choornam* had been subjected to various studies to establish the works of Siddhars to be true. Literary collections, physicochemical and Phytochemical analysis, toxicological study, pharmacological study and clinical study are done to prove the anti – ulcer activity of *milagathi choornam.*

1. Finished form of *Milakathi Choornam* (MC)

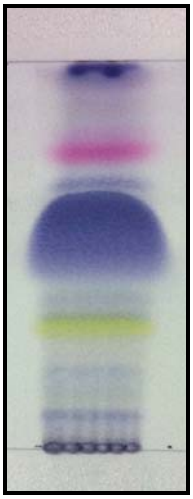
The MC was prepared following strictly the method mentioned in the Siddha text. The finished MC gave positive results to all tests for *Choornam* as mentioned in Siddha Gunapadam literature.

2. PHYSICO-CHEMICO ANALYSIS

Table 1: Physicochemical parameters

S.No	Parameter	Mean Value
1.	Loss on Drying at 105°C	7.475 %
2.	Total Ash	11.775 %
3.	Acid insoluble Ash	0.175 %
4.	Water Soluble Extractive	28.8 %
5.	Alcohol Soluble Extractive	31.9 %
6.	Particle size	Completely passes through sieve no.44
7.	pH	6.5

TLC analyses

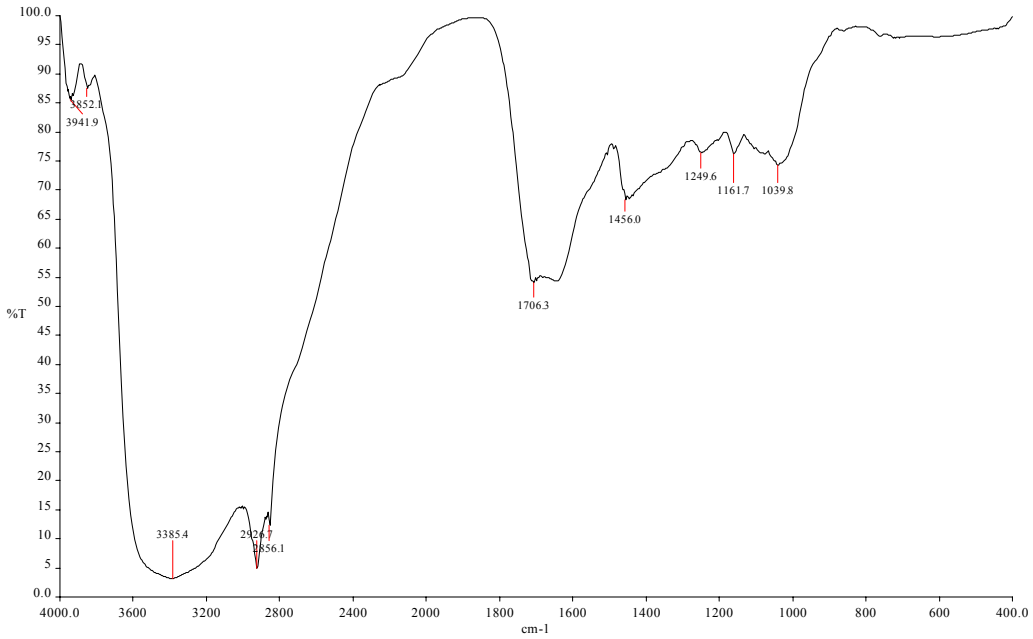


After spray with visualizing agent

Sl.No	After Dipping in Vanillin-Sulphuric acid	
	Rf value	**Colour of the spot**
1	0.08	Purple
2	0.20	Purple
3	0.31	Yellow
4	0.38	Purple
5	0.58	Violet
6	0.68	Purple
7	0.77	Pink
8	0.95	Purple

The above result shows the presence of eight active compounds and at 0.38 Rf there is a higher concentration of active compound. This fingerprint may be used for standardization purpose in future.

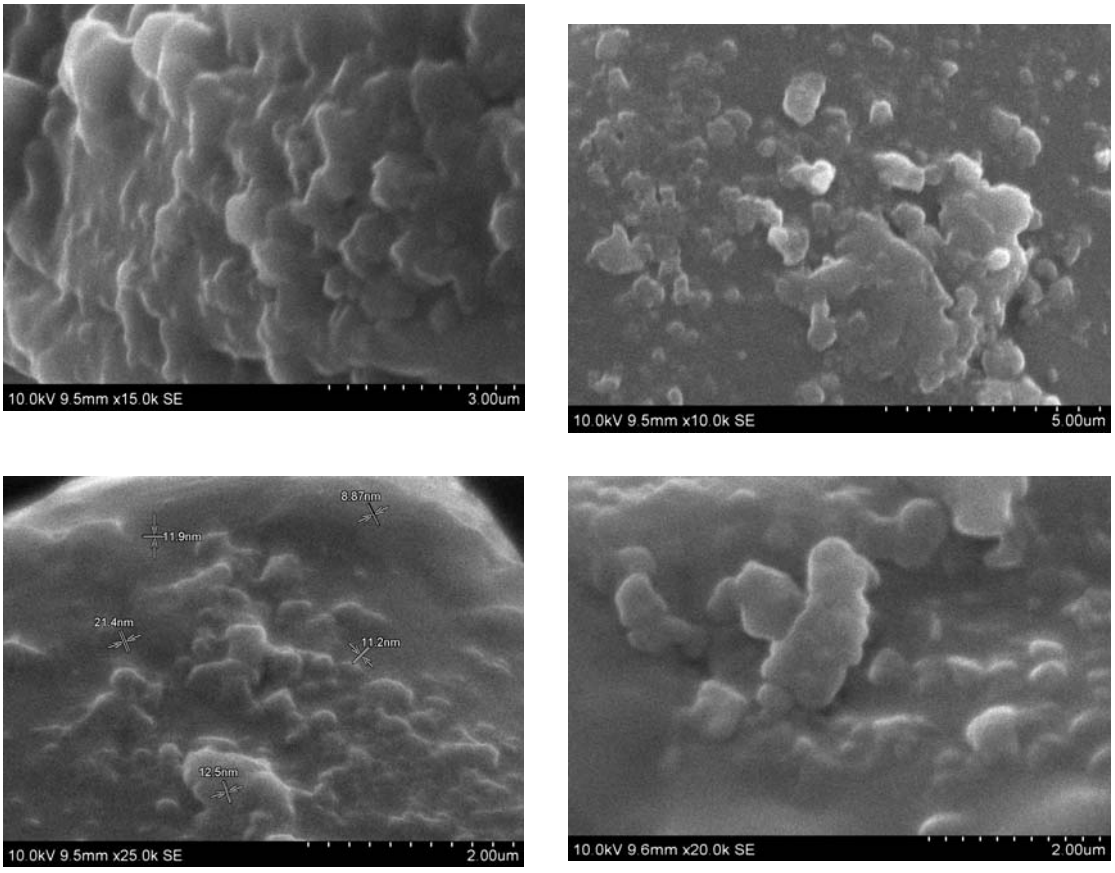
FTIR RESULTS



Frequency bands	Functional group
3385	Amine N- H stretch
2924	Alkyl c-h stretch
2856.1	Aromatic c-c Bending
1706.3	Aldehyde C=O Stretch
1456	Aromatics C-C stretch
1249.6	Alkyl halides C-H wag

These bands indicate the presence of amines, aldehydes, carboxylic acid, alkynes, and aromatic functional groups

SCANNING ELCTRON MICROSCOPE (SEM) IMAGES



The above plates indicates that all the particles are in nano level. This particle size makes. the choornam for better absorption.

For drug delivery biodegradable nano particle formulations are needed as it is the intention to transport and release the drug in order to be effective.

TABLE 2: PHYTOCHEMICAL ANALYSIS OF *MILAGATHI CHOORNAM*

Qualitative Phytochemical Tests		
1.	Alkaloids	+ ve
2.	Anthraquinones	- ve
3.	Volatile oil	+ ve
4.	Tannins	+ ve
5.	Steroids	+ ve
6.	Saponin	- ve
7.	Flavonoids	+ ve

Phytochemical Analysis shows presence of alkaloids, volatile oil, flavonoids and steroids.

Tannins are known to ‘ tan’ the outer most layer of the mucosa and to render it less permeable and more resistant to chemical and mechanical injury or irritation.(Asuzu and Onu et al., 1990)

Flavonoids have been found to be free radical scavengers. (Baumann et al., 1980). Free radicals play an important role in ulcerative an erosive lesions of the gastro intestinal tract. In relation to their low toxicity and to the properties reported, flavonoids could have a therapeutic potential ideal for treatment of gastro intestinal diseases associated with Helicobacter pylori infection i.e., type B gastritis and duodenal ulcer.(Di Carlo et al. 1999).

Saponin increases the amount of glucose in ethanol -induced gastric ulceration. (Marhuenda et al., 1994)

TABLE 3: PRELIMINARY CHEMICAL ANALYSIS OF *Milagathi Choornam*

S.No.	EXPERIMENT	RESULT
1	Reducing sugar	-
2	Starch	-
3	Protein	-
4	Amino acid	-
5	Albumin	+
6	Phosphate	+
7	Sulphate	+
8	Chloride	+
9	Iron	+
10	Calcium	+
11	Sodium	-
12	Potassium	-
13	Zinc	-
14	Magnesium	-
15	Alkaloids	-
16	Tannic acid	+

Chemical analysis of the MC shows the presence of tannic acid,calcium, iron,chloride,sulphate,phosphate,albumin. Tannic acid inhibits the gastric acid secretion in pylorous ligated rats and mice. (Makato Muramatue et al., 1992). Phosphate is essential for formation of energy bonds like ATP, ADP. (Ambika shanmugam, Fundamentals of BioChemistry, page no.534)

H.pylori infection was associated with a 40% increase in the prevalence of iron deficiency.(V.M Cardenes et al., 2005)

3. TOXICOLOGICAL AND PHARMACOLOGICAL STUDIES

3.1 ACUTE TOXICITY PROFILE

Table 4: Dose finding experiment and its behavioral Signs of Toxicity

No	Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	2000	+	+	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	5000	+	+	-	+	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-

1. Alertness 2. Aggressiveness 3. Pile erection 4. Grooming 5. Gripping 6. Touch Response 7. Decreased Motor Activity 8. Tremors 9. Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14. Analgesia 15.Lacrimation 16. Exophthalmos 17. Diarrhoea 18. Writhing 19. Respiration 20. Mortality

MC at the dose of 5000mg/kg/po did not exhibit mortality and did not show any signs of acute toxicity and significant behaviour changes. As per OECD 425 guidelines, the median lethal dose is said to be more than 5000 mg/kg.

Table 5. Body weight of rats in the toxicity study of the Milakathi Chooranam.

Body Weight (g)	Control	MC 5000 mg/kg
Day 0	174±10.2	182±10.1
Day 7	178±5.9	185±12.1
Day 14	181±11.2	188±12.5
Mortality	Nil	Nil

Results are expressed as mean ± S.E.M. n=6

3.2 SUB ACUTE TOXICITY PROFILE

Animals were not shown any significant toxic clinical signs during the dosing period of 28 days. All animals from control and all the treated dose groups survived throughout the dosing period of 28 days. Results of body weight determination of animals of control and different dose groups exhibited comparable body weight gain but at the 100mg treated group showing significant body weight reduction after two weeks of treatment. During dosing period, the quantity of food consumed by animals from different dose groups was found to be comparable and normal with that of control animals. Ophthalmoscopic examination of animals in control and Milakathi Chooranam treated groups did not reveal any major and remarkable abnormality. Results of Biochemical investigations revealed the values obtained were within normal biological and laboratory limits. The results of haematological investigations conducted on day 28, revealed increase in eosinophil and platelet level and decrease in monocyte at high dose group when compared to control; and the increase or decrease in the values obtained was within normal biological and laboratory limits.

Urine analysis data of control group and treated group of animals did not reveal any abnormalities. Comparison of organ weights of Milakathi Chooranam treated animals with respective control animals showed statistically significant weight gain in kidney ($P<0.01$) and lung ($P<0.05$) on day 28. Gross pathological examination of animals in control as well as the treated groups did not reveal any major abnormalities.

Based on the results obtained, it can be concluded that no significant toxic effect was observed upto 400mg/kg of Milakathi Chooranam treated via oral route over a period of 28 days. So, the Milakathi Chooranam can be prescribed for therapeutic use in human with the dosage recommendations of upto 400mg/kg. body weight p.o.

Table 6: Body weight changes of rats treated with Milakathi Chooranam during 28 days of sub acute toxicity study

Days	Group			
	Control	**Milakathi Chooranam 100/kg**	**Milakathi Chooranam 200/kg**	**Milakathi Chooranam 400g/kg**
0	151.2±5.2	142.8±4.2	140.1±4.1	160.4±5.0
7	154.4±4.4	142.1±5.1	142.3±4.0	162.2±4.5
14	156.5±5.0	135.0±3.6**	145.6±3.2	164.0±4.0
28	159.2±6.2	138.2±3.4*	148.2±4.2	166.2±4.8

The Data are expressed as mean ± S.E.M. Significant difference in each group versus the control were as follow *p<0.05, **P<0.01.

Table 7: Effect of Milakathi Chooranam on heamatological parameters after 28 days treatment

Parameter	Normal	Milakathi Chooranam 100/kg	Milakathi Chooranam 200/kg	Milakathi Chooranam 400g/kg
RBC (millions/cu.mm)	5.10±0.43	5.12±0.34	5.20±0.32	5.42±0.40
Hb (g/dl)	14.01±0.72	14.33±0.98	14.0±1.2	14.20±1.0
PCV (%)	42.18±1.21	44.7±2.1	44.4±2.2	45.0±2.18
WBC(cells/cu.mm)	7375±340	7250±334	7325±455	7633±510
Neutrophil (%)	54.41±4.24	52.23 ±2.5	49.4±3.8	52.32±3.2
Lymphocytes (%)	4.9±2.48	5.2±3.0	4.8±3.1	4.6±4.1
Eosinophil's (%)	4.0±0.42	5.1±0.51	5.4±0.44	5.63±0.40*
Monocytes (%)	4.0±0.02	3.0±0.24**	4.0±0.3	2±0.1**
Basophils (%)	0±0	0±0	0±0	0±0
Platelet Count (10^5 cells/cu.mm)	1.72±0.05	1.80±0.04	1.84±0.05	2.0±0.08**
MCV (Fl/red cell)	79.7±2.8	80.2±1.5	83.4±2.0	84.2±4.0
MCHC (pg/red cell)	25.1±1.8	24.84±1.4	25.6±1.2	27.10±2.0

Results are expressed as mean ± S.E.M. n=6; *P<0.05; **p<0.01 as compared to the control

Table 8: Effect of Milakathi Chooranam on Blood Chemistry values of rats after subacute toxicity study

Parameter	Control	Milakathi Chooranam treated group	
		200 mg/kg	400 mg/kg
Glucose (mg/dL)	72.22±6.27	68.25±7.53	69.41±5.32
Creatinine (mg/dL)	0.90±0.06	0.87±0.05	0.93±0.03
TB (mg/dL)	0.67±0.05	0.65±0.06	0.62±0.05
AST (IU/L)	132.1±7.36	125±6.30	127.2±6.14
ALT (IU/L)	37.13±3.52	32.12±2.75	30.10±2.21
ALP (IU/L)	78.30±4.40	74.69±4.45	66.32±4.32
TC (mg/dL)	56.72±5.22	55.05±5.52	55.74±5.12
TP (g/dL)	8.18±0.20	7.89±0.20	7.48±0.72
Albumin (g/dL)	2.64±0.07	2.75±0.07	2.72±0.06

Results are expressed as mean ± S.E.M. n=6; $^{ns}P>0.05$ as compared to the control.

Table 9: Urine Analysis

Parameters	Control	Milakathi Chooranam 100/kg	Milakathi Chooranam 200/kg	Milakathi Chooranam 400g/kg
Colour	Yellow	Yellow	Yellow	Yellow
Transparency	Clear	Slightly turbid	Slightly cloudy	Slightly turbid
Specific gravity	1.010	1.010	1.010	1.010
PH	>7.2	>8.0	>8.0	>9.0
Protein	Nil	3+	3+	3+
Glucose	Nil	Nil	Nil	Nil
Bilirubin	-ve	-ve	-ve	-ve
Ketones	-ve	+ve	+ve	+ve
Blood	Absent	Absent	Absent	Absent
Urobilinogen	Normal	Abnormal	Abnormal	Abnormal
Pus cells	0-cells/HPF	1-cell/HPF	2-cells/HPF	1-cell/HPF
RBCs	Nil	Nil	0-1cells/HPF	Nil
Epithelial cells	Nil	1-cell/HPF	Nil	1-cell/HPF
Crystals	Nil	Nil	Nil	Nil
Casts	Nil	Nil	Nil	Nil
Others	Bacteria seen	Bacteria seen	Bacteria seen	Bacteria seen

Table 10. Organ weight changes of rats in the sub acute toxicity study of the Milakathi Chooranam.

Parameter	Normal Control	Milakathi Chooranam 100/kg	Milakathi Chooranam 200/kg	Milakathi Chooranam 400g/kg
Heart	0.35±0.02	0.37±0.02	0.34±0.01	0.35±0.02
Liver	4.2±0.26	3.94±0.18	3.96±0.21	4.25±0.31
Kidney	1.68±0.04	1.65±0.03	1.96±0.04**	1.77±0.05
Lung	0.52±0.02	0.53±0.03	0.64±0.04*	0.58±0.03
Brain	1.74±0.06	1.66±0.04	1.68±0.03	1.72±0.05

Results are expressed as mean ± S.E.M. n=6; *P<0.05; **p<0.01 as compared to the control

3.3 PHARMACOLOGICAL EVALUATION OF *MILAGATHI CHOORNAM*

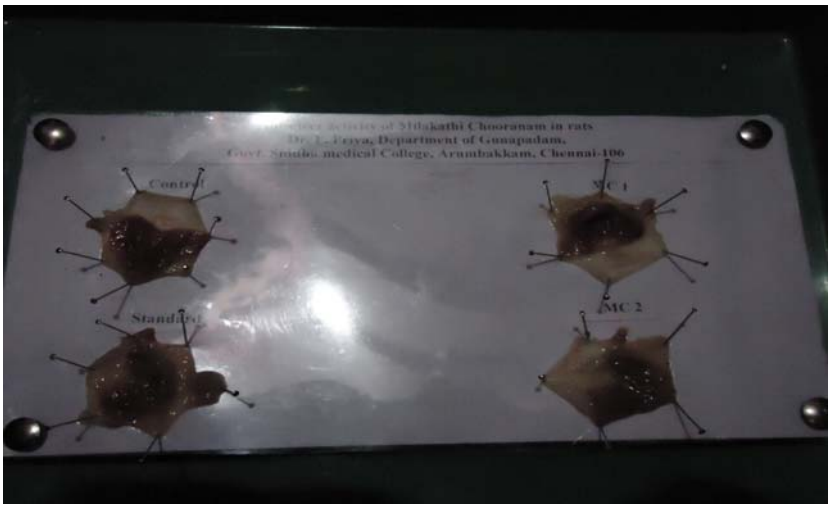
Ulcers are crater-like erosion or sore that occur in the upper gastrointestinal tract of the body. Stomach ulcers are also called peptic ulcers. The word peptic refers to pepsin, a stomach enzyme that breaks down protein. A peptic ulcer located in the stomach is called a gastric ulcer. An ulcer is the result of an imbalance between aggressive and defensive factors. On one hand, too much acid and pepsin can damage the stomach lining and cause ulceration. On the other hand, the damage comes first from some other cause making the stomach lining susceptible to even an ordinary level of gastric acid. Peptic ulceration is a very common disease and it is estimated that approximately 10%-20% of the adult male population in western countries will experience a peptic ulcer at some stage in their lives.

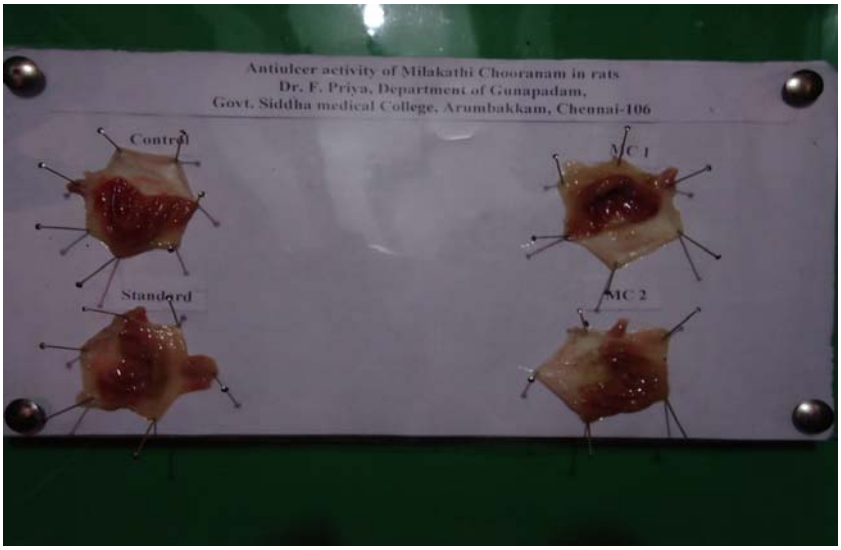
Peptic ulcer is a benign lesion of gastric or duodenal mucosa occurring at a site where the mucosal epithelium is exposed to acid and pepsin. There is constant confrontation in the stomach and upper small bowel between acid-pepsin aggression and mucosal defense. Usually, the mucosa can withstand the acid-pepsin attack and remain healthy. That is, a mucosal ‘‘barrier’’ to back diffusion of acid is maintained. However, an excess of acid production or an intrinsic defect in the barrier functions of the mucosa can allow the defense mechanism to fail and ulcer to result. Since it’s recognition of the peptic ulcer as an important chemical entity, various efforts have been made to find suitable remedial measures. For several decades the adage ‘‘no acid-no ulcer’’ and the drugs used to reduce acid secretion have dominated the pharmacological basis of ulcer therapy. It is now well established that peptic ulcer disease can be prevented by strengthening the defensive mechanisms of gastric and duodenal mucosa rather than attenuating factors of aggression causing ulceration.

Histopathology of stomach show that test drug Milagathi Chooranam 500 mg/kg significantly reduced gastric lesion formation and sub-mucosal edema similar to the ranitidine treated animals but it was not remarkable as standard drug treated group. Careful evaluation revealed that the mucosa of ulcer control animals have hemorrhagic erosion, discontinuity in the lining of epithelium cells and significant damage in sub-mucosa.

Normal mucosa with small strophic gland, mild hyperplasia and no edema were observed for animals treated with ranitidine. Similarly, the effect was moderate at the lower dose. Mucosa of animals treated with Milakathi Chooranam 250mg/kg was identified with hemorrhagic erosion, discontinuity in the lining of epithelium cells and significant damage in sub-mucosal layer. Thus our study reveals that the significant antiulcer effect of Milakathi Chooranam. However, further studies are required to establish its exact mode of action and the active principles involved in its anti-ulcer effect.

From this study, it is clearly evident that Milakathi Chooranam have significant action as anti-ulcer activity in animal models at the dose levels of 250 and 500mg/kg^{-1}.

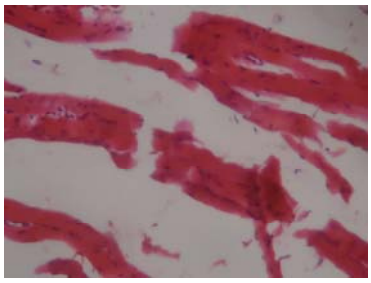
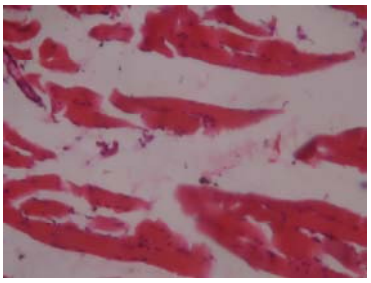
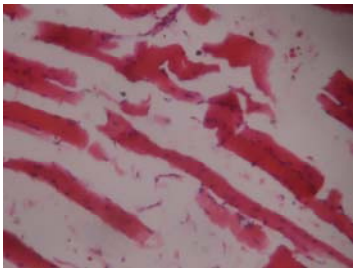





Antiulcer activity of Milakathi Chooranam in rats
Dr. F. Priya, Departme
Govt. Siddha medical
Control
MC 1
Standard
MC 2

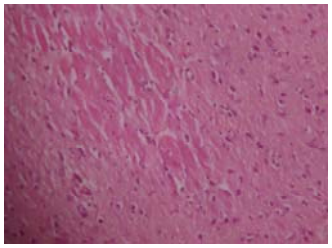
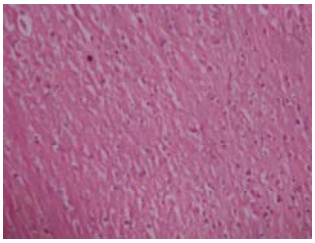
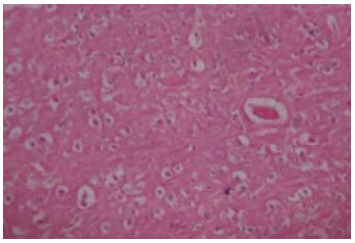
HIOSTOTATHALOGICAL PICTURES

BONES

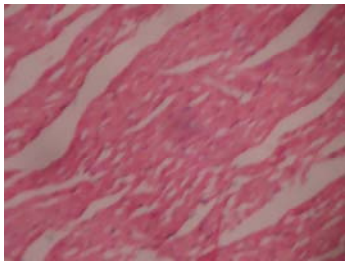
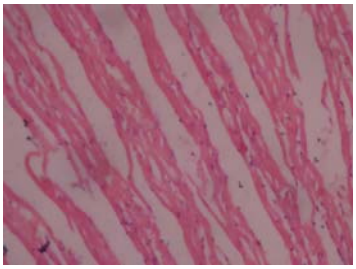
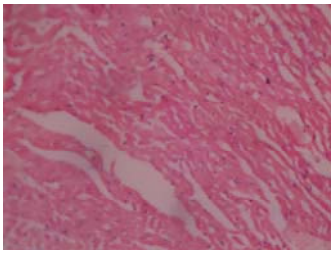




100mg 200mg 400mg

BRAIN

HEART 100mg 200mg 400mg

100mg 200mg 400mg

INTESTINE

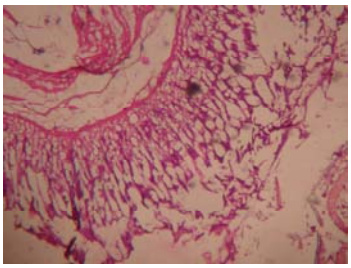
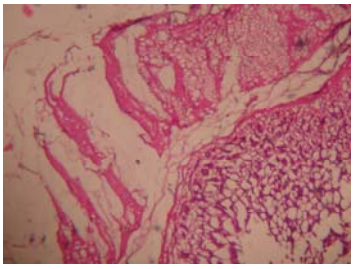
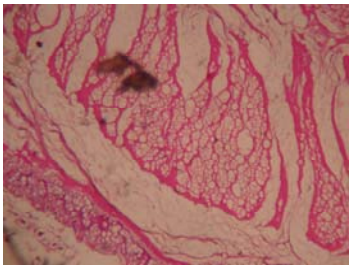




Table 11 — Effect of Milakathi Chooranam on ulcer index

Groups	Ulcer index
Normal	1.25±0.08
CMC control	24.19 ± 0.26
MC (250mg/kg)	19.64 ± 0.22^{**,b}
MC (500mg/kg)	14.26 ± 0.18^{**,b}
Ranitidine (60mg/kg)	10.34 ± 0.15^{**,b}

Values are the mean ± S.E.M. (n=6).

Significance *p <0.05, **p<0.01 Vs Control.; ^{b}p<0.01 Vs Standard

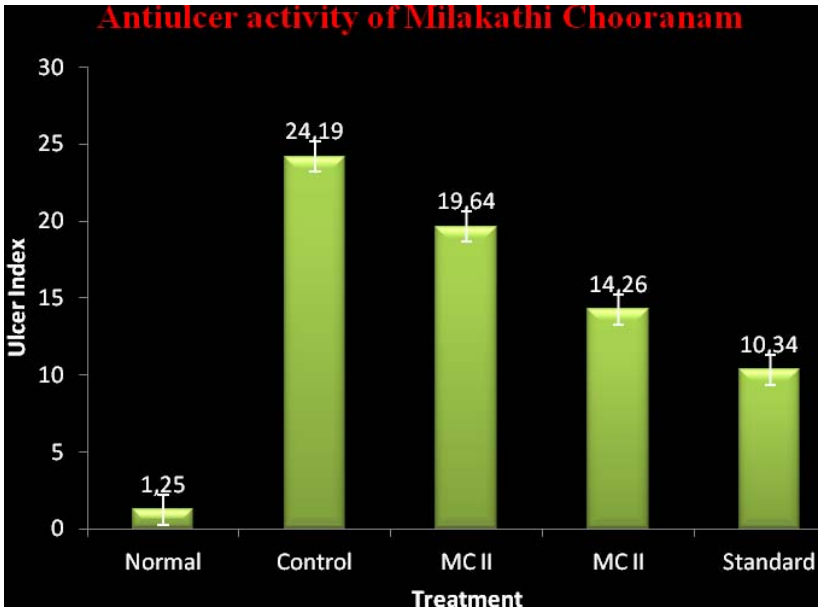
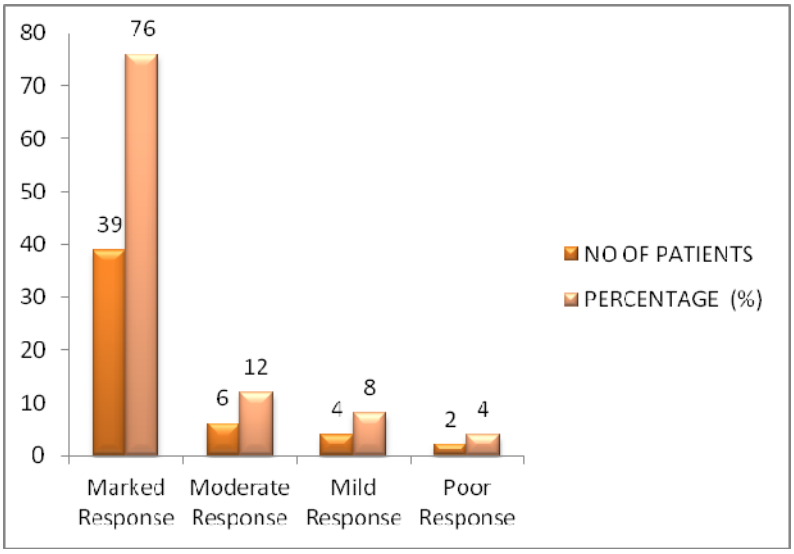


Table No.4.5.1

Gradation result

SL. NO	LEVEL OF IMPROVEMENT	NO.OF PATIENTS	PERCENTAGE (%)
1	Marked Responese	39	76
2	Moderate Responese	6	12
3	Mild Responese	4	8
4	Poor Responese	2	4
TOTAL		51	100



Inference:

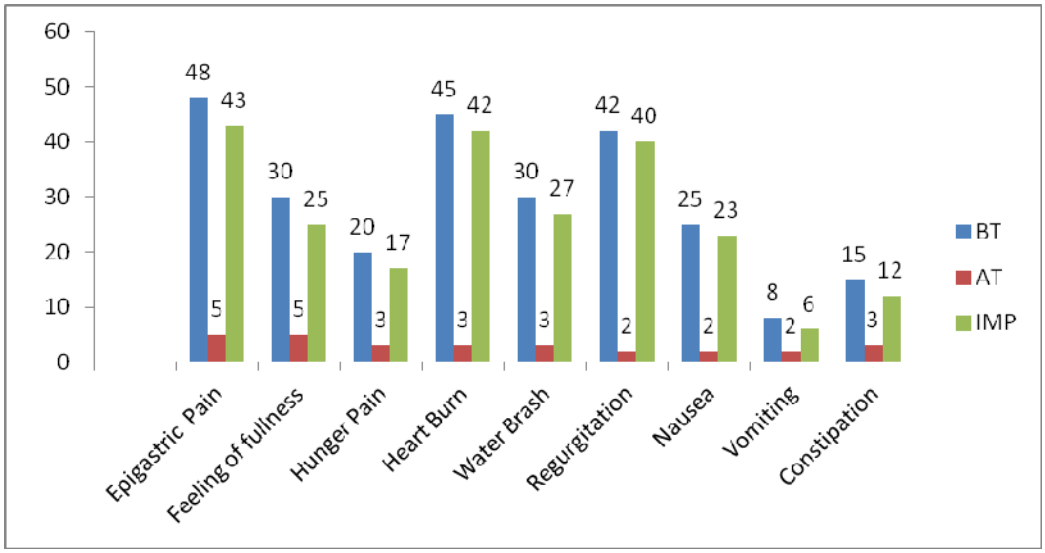
Among 51 patients,

- 39 patients had marked response.
- 6 patients had moderate respone.
- 4 patients had mild response.
- 2 patients had poor response.

Table NO.4.5.2

Improvement In Signs And Symptoms

SL.NO	SIGNS AND SYMPTOMS	No of Patients			
		BT	AT	IMP	IMP %
1	Epigastric Pain	48	5	43	90
2	Feeling of fullness	30	5	25	83
3	Hunger Pain	20	3	17	85
4	Heart Burn	45	3	42	93
5	Water Brash	30	3	27	90
6	Regurgitation	42	2	40	95
7	Nausea	25	2	23	92
8	Vomiting	8	2	6	75
9	Constipation	15	3	12	80



Inference:

Among 51 patients,

43 out of 48 relieved from epigastric pain 27 out of 30 relieved from water brash

25 out of 30 relieved from feeling of fullness 40 out of 42 relieved from regurgitation

17 out of 20 relieved from hunger pain 23 out of 25 relieved from nausea

42 out of 45 relieved from heart burn 12 out of 15 relieved from constipation

SUMMARY

Herbo- mineral drug *Milagathi choornam was* prepared as per Siddha classical way and its efficacy on peptic ulcer was evaluated.

The literary review in Siddha and modern aspect are discussed thoroughly and the valuation of drug had been established.

Studies involving phytochemical, chemical, elemental and physio chemical analysis are done to make its efficiency more visible.

The pharmacological analysis showed that the drug has got significant Anti ulcer activity with cytoprotective mechanism.

In clinical study the drug has showed 76% marked response to peptic ulcer.

This present study confirms that *Milagathi choornam has* remarkable Anti ulcer activity and prooves the words written in Siddha literature are evergreen.

The trial drug was duely identified and authenticated by the gunapadam experts. The literary reviews along with Phytochemical, chemical constituents, elemental analysis supports the efficient activity of the drug, Standardisation of the drug was done by physio chemical analysis.

Presence of flavanoids, alkaloids, saponins, tannins, helps in healing ulcer.

Presence of Tannic acid, chloride, Calcium, Ferrous, Phosphate, and sulphate aids in mucosal protection and heals ulcer.

Through above supportive theories of *Milagathi choornam,* it can be concluded that the drug throw new light on *Siddha* system and Peptic ulcer disease

CONCLUSION

Inspite of long usage of *Milakathi choornam* in our Siddha medicine, no evidences in safety and therapeutic applications are not documented yet. These studies pave the pathway in validation of MC in the treatment of Peptic Ulcer and make the scientific communities to believe the Siddha medicine.

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16. Aviyalikum amutha surakkam
17. Agathiyar attavanai vagadam
18. Agathiyar kalaizhanam
19. Pathinen siddharkal nadi sasthiram
20. Vaidya thiratu.
21. Vaidya sathagam.
22. Pathartha guna villakam
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24. Theriyar venba.
25. Danvadri nigandu

26. Valluvar cinthamani

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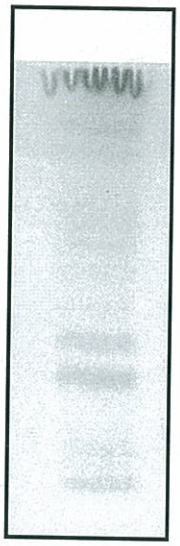
15.01.2013

Name of the student: Dr. F. Priya, Govt Siddha Medical College, Chennai-106

REPORT OF KADUKKAI CHOORANAM

S.No	Parameter	Mean Value
1.	Loss on Drying at 105°C	5.3 %
2.	Total Ash	3.0 %
3.	Acid insoluble Ash	0.3 %
4.	Water Soluble Extractive	53.7 %
5.	Alcohol Soluble Extractive	59.6 %
6.	Particle size	Completely passes through sieve no.44
7.	pH	6.0
Qualitative Phytochemical Tests		
1.	Alkaloids	- ve
2.	Anthraquinones	- ve
3.	Tannins	+ ve
4.	Flavonoids	- ve
5.	Steroids	+ ve
6.	Saponin	+ ve
7.	Phenol	+ ve
TLC		As Below



After spray with visualizing agent

Sl.No	After Dipping in Vanillin-Sulphuric acid	
	Rf value	Colour of the spot
1	0.09	Grey
2	0.26	Blue
3	0.34	Blue
4	0.41	Grey
5	0.46	Blue
6	0.57	Blue
7	0.60	Purple
8	0.64	Grey
11	0.79	Purple
12	0.83	Purple

Solvent system:

Toluene : Ethyl acetate: Acetic acid (5 : 5 : 0.5).

TLC plate:

Aluminium plate precoated with silica gel $60F_{254}$ of 0.2 mm thickness (Merck).

Developing chamber:

Camag's twin trough chamber.

Visualizing reagent:

Vanillin-sulphuric acid reagent.

Extract Preparation:

4 g of the chooranam was soaked overnight in chloroform. Boiled on a water bath for 10 mins, filtered and concentrated to 10 ml.

Procedure:

The extract was applied on the TLC using capillary and developed in the solvent system. The developed TLC plate was air dried and photograph was taken in white light. Then dipped in vanillin-sulphuric acid reagent, heated in an oven at 105°C until the development of coloured spots and photograph taken.

REPORT OF MILAGATHI CHOORANAM

S.No	Parameter	Mean Value
1.	Loss on Drying at 105°C	7.475 %
2.	Total Ash	11.775 %
3.	Acid insoluble Ash	0.175 %
4.	Water Soluble Extractive	28.8 %
5.	Alcohol Soluble Extractive	31.9 %
6.	Particle size	Completely passes through sieve no.44
7.	pH	6.5
Qualitative Phytochemical Tests		
1.	Alkaloids	+ ve
2.	Anthraquinones	- ve
3.	Volatile oil	+ ve
4.	Tannins	+ ve
5.	Steroids	+ ve
6.	Saponin	- ve
7.	Flavonoids	+ ve
TLC		As Below

After spray with visualizing agent

Sl.No	After Dipping in Vanillin-Sulphuric acid	
	Rf value	Colour of the spot
1	0.08	Purple
2	0.20	Purple
3	0.31	Yellow
4	0.38	Purple
5	0.58	Violet
6	0.68	Purple
7	0.77	Pink
8	0.95	Purple

Solvent system:

Toluene : Ethyl acetate (6:1.5).

TLC plate:

Aluminium plate precoated with silica gel $60F_{254}$ of 0.2 mm thickness (Merck).

Developing chamber:

Camag's twin trough chamber.

Visualizing reagent:

Vanillin-sulphuric acid reagent.

Extract Preparation:

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(R.Shakila)
Research Officer (Chemistry)

(S. Jega Jothi Pandian)
Research Officer (Scientist 2) I/c

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Grams: "AYUSH" CHENNAI

1st June 2012

CERTIFICATE

Certified that the Fruit submitted for identification by Dr. **F. Priya**, III year P.G. Gunapadam, Government Siddha Medical College, Chennai is identified as ***Terminalia chebula Retz.*** Fam. Combretaceae.

Sasikala Ethirajulu
Asst. Director (Pharmacognosy)

S. Jega Jothi Pandian
Asst.Director Incharge

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

69, Anna Salai, Guindy, Chennai-600 032

This Certificate is awarded to Dr/~~Mr/Mrs~~ F. PRIYA B.S.M.S

for participating in the Workshop on

'Introduction to Scientific & Medical Writing'

organized by the Department of Epidemiology,
The Tamil Nadu Dr. M.G.R. Medical University on 18th March, 2011.

This educational activity has been awarded ***10 Credit Points***
by the Centre for Accreditation, The Tamilnadu Dr. M.G.R. Medical University.

Dr. N. KABILAN, M.D. (Siddha)
HOD i/c, DEPT. OF EPIDEMIOLOGY

Dr. SUDHA SESHAYYAN, M.S.
REGISTRAR (FAC)

Dr. MAYIL VAHANAN NATARAJAN
M.S.Orth. M.Ch.Orth. (L'pool) Ph.D. D.Sc. F.R.C.S. D.Sc. (Hon)[3]
VICE CHANCELLOR

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL,CHENNAI-600106

CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all details about the study in the terms readily understood by the patient and handed over a copy of the patient information sheet.

Date:

Signature of the investigator

Name

CONSENT BY PATIENT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial and the nature of drug treatment and follow-up, including the laboratory investigations to be performed to monitor and safeguard my body functions.

I am also aware of my right to opt out of the trial at any time during the course of trial without having to give the reasons for doing so. I, exercising my free power of choice, hereby give my consent to be included as a subject in the clinical trial of traditional remedy, namely *KADUKKAI CHOORANAM* for the treatment of Obesity. I understand that I may be treated with this drug for the disease.

Signature of the attending Physician

Name and Signature of the Patient

Place :

Name and Signature of witness

Date :

Relationship to patient: _____

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL, CHENNAI-106

BRANCH-II M.D. (SIDDHA) GUNAPADAM

NAME OF THE DISEASE : **OBESITY**

NAME OF THE MEDICINE : ***KADUKKAI CHOORNAM***

DOSE : **1gm bd with warm water**

O.P No:	**Date:**	**Height:**
Name:	**Age/Sex:**	**Weight:**
Address:		**BP:**
Occupation:	**Marital status:**	**PR:**

SIGNS & SYMPTOMS	**WEEKS**						
	0	**2**	**4**	**6**	**8**	**10**	**12**
Weight							
BMI							
Abdominal circumference							
Waist-hip ratio							
Others							
Signature of M.O							

ASSESSMENT

BMI	Before treatment	After treatment

LAB INVESTIGATIONS

Sample		Before treatment	After treatment
BLOOD	DC		
	TC		
	ESR		
	Hb		
	Blood sugar		
	Lipid profile Total cholesterol Triglycerides HDL LDL VLDL		
URINE	Albumin		
	Sugar		
	Deposit		

ENVAGAI THERVUGAL

SIDDHA INVESTIGATION	BEFORE TREATMENT	AFTER TREATMENT (IN WEEKS)						
		1	2	3	4	5	6	7
NAA								
NIRAM								
MOZHI								
VIZHI								
MALAM								
MOOTHIRAM								
SPARISAM								
NAADI								
NEERKURI								
NEIKURI								
OTHERS								

தேக இலக்கணம்

Before treatment

வாதம்	பித்தம்	கபம்
மெலிந்து உயர்ந்த உடல் ☐	ஊண் குறைந்த உடல் ☐	கொழுமை ☐
கருமை நிறம் ☐	வெண்மை நிறம் ☐	சிவப்பு நிறம் ☐
முனை பிளந்த தலைமயிர் ☐	அற்ப உண்டி ☐	குமுறலான குரலோசை ☐

தூக்கம் கெடல் ☐	சொற்ப நித்திரை ☐	மிகு தூக்கம் ☐
கார சுவையில் விருப்பம் ☐	புளிப்பு சுவையில் விருப்பம் ☐	இனிப்பு சுவையில் விருப்பம் ☐
உடல் இளைத்து கருத்தல் ☐	கண், மலம், சிறுநீர், தோல் ☐ இவை மஞ்சள் நிறமடைதல்	உடல் கனமாக தோன்றுதல் ☐
உடல் நடுக்கல் ☐	உடல் முற்றும் எரிச்சல் ☐	உடல் முற்றும் உள்ள கட்டுகள் தளரல் ☐
வன்மை குறைதல் ☐	பசி, நீர்வேட்கை மிகுதிப்படல் ☐	ஊக்கம் குறைதல் ☐

After treatment

வாதம்	பித்தம்	கபம்
மெலிந்து உயர்ந்த உடல் ☐	ஊண் குறைந்த உடல் ☐	கொழுமை ☐
கருமை நிறம் ☐	வெண்மை நிறம் ☐	சிவப்பு நிறம் ☐
முனை பிளந்த தலைமயிர் ☐	அற்ப உண்டி ☐	குமுறலான குரலோசை ☐
தூக்கம் கெடல் ☐	சொற்ப நித்திரை ☐	மிகு தூக்கம் ☐
கார சுவையில் விருப்பம் ☐	புளிப்பு சுவையில் விருப்பம் ☐	இனிப்பு சுவையில் விருப்பம் ☐
உடல் இளைத்து கருத்தல் ☐	கண், மலம், சிறுநீர், தோல் ☐ இவை மஞ்சள் நிறமடைதல்	உடல் கனமாக தோன்றுதல் ☐
உடல் நடுக்கல் ☐	உடல் முற்றும் எரிச்சல் ☐	உடல் முற்றும் உள்ள கட்டுகள் தளரல் ☐
வன்மை குறைதல் ☐	பசி, நீர்வேட்கை மிகுதிப்படல் ☐	ஊக்கம் குறைதல் ☐

Signature of Medcial Officer

Signature of the student

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL,CHENNAI-600106

CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all details about the study in the terms readily understood by the patient and handed over a copy of the patient information sheet.

Date:

Signature of the Investigator

Name:

CONSENT BY PATIENT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial and the nature of drug treatment and follow-up, including the laboratory investigations to be performed to monitor and safeguard my body functions.

I am also aware of my right to opt out of the trial at any time during the course of trial without having to give the reasons for doing so. I, exercising my free power of choice, hereby give my consent to be included as a subject in the clinical trial of traditional remedy, namely *Milagathi choornam* for the treatment of ulcer. I understand that I may be treated with this drug for the disease.

Signature of the attending Physician

Name and Signature of the Patient

Place :

Name and Signature of witness

Date :

Relationship to patient: _____

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL, CHENNAI-600106

BRANCH-II M.D. (SIDDHA) GUNAPADAM

NAME OF THE DISEASE : PEPTIC ULCER (GUNMAM)

NAME OF THE MEDICINE:*MILAGATHI CHOORANAM*

DOSE : 1gm bd with food

O.P. NO		ADDRESS
DATE		
NAME		
AGE/SEX		
OCCUPATION		
RELIGION/MARITAL STATUS		

VITAL SIGNS:

Weight :

Height :

Heart Rate :

Pulse Rate :

Respiratory Rate :

SYMPTOMS	BEFORE TREATMENT	AFTER TREATMENT(IN WEEKS)						
		1	2	3	4	5	6	7
EPIGASTRIC PAIN								
FEELING OF FULLNESS								
HUNGER&EMPTY FEELING								
HEART BURN								
WATER BRASH								
REGURGITATION								

NAUSEA/VOMITING								
CONSTIPATION								
BLOODY(OR)DARK STOOL								
HEMATEMESIS								
SIGNATURE OF MO/HOD								

LAB INVESTIGATION	BEFORE TREATMENT	AFTER TREATMENT
BLOOD: DC		
TC		
ESR(1/2hr / 1 hr)		
HB		
SUG(F/PP/RAN)		
BLOOD GROUP		
ELISA		
UREASE TEST		
BREATH TEST		
ENDOSCOPIC STUDY		
BARIUM X-RAY		
STOOL-OCCULT BLOOD		
URINE; ALBUMIN		
SUGAR		
DEPOSITS		

SIDDHA INVESTIGATION	BEFORE TREATMENT	AFTER TREATMENT(IN WEEKS)						
		1	2	3	4	5	6	7
NAA								
NIRAM								
MOZHI								
VIZHI								
MALAM								
MOOTHIRAM								
SPARISAM								
NAADI								
NEERKURI								
NEIKURI								
OTHERS								

SIGNATURE OF MO

SIGNATURE OF HOD